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ROENTGENOGRAPHIC INTERPRETATION OF ACUTE HEMATOGENOUS OSTEOMYELITIS TREATED WITH PENICILLIN*

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PENICILLIN has revolutionized the management of acute hematogenous osteomyelitis.[1] The spectacular control of the bacteriemia, the bony infection, and the metastatic visceral infectious complications has produced a radical reduction in morbidity as well as mortality. This control of the infection has been so effective that emergency surgical decompression of the area of involved bone has not become necessary except in fulminating cases. Instead, the required surgery has usually been limited to incisions and drainage of abscesses developing in soft tissues and to the removal of selected large and unabsorbed sequestra. The disfiguring sequelae such as deformity, limp, draining sinuses, or ankylosis of adjacent joints have been largely eliminated. Likewise, a careful study of the cases treated with penicillin has forced us to modify our earlier conceptions and interpretations of the roentgenographic changes occurring in acute hematogenous osteomyelitis.

MATERIAL

During the past twenty-seven months we have observed the results of treatment with penicillin in 52 cases of acute hematogenous osteomyelitis. The group included 44 cases of acute hematogenous osteomyelitis of the major long bones, some of which also had involvement of the flat bones of the pelvis. In addition, there were 4 cases with involvement of the pelvic bones only. The responsible etiologic agent was determined in every instance but 4, and was found to be the hemolytic *Staphylococcus aureus* in 42 cases, the nonhemolytic *Staphylococcus albus* in 3, the hemolytic streptococcus in one, and the pneumococcus type III in one.

METHOD

All of the cases were treated primarily with penicillin although 28 of the patients had received a limited amount of sulfonamide therapy before penicillin was started. In 9 of these, penicillin and sulfadiazine

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were given concurrently. Many of the early cases received less than 800,000 units and the results were usually very good. Experience, however, has shown[1] that a total dose of 1,500,000 or more units administered over a period of approximately three or more weeks is a desirable dosage. The penicillin was usually administered intravenously or intramuscularly in amounts of 15,000 to 25,000 units at intervals of three hours. In some instances, it was administered by continuous intravenous drip when 30,000 to 80,000 units in 2,000 cc. of physiological saline solution were administered at a rate of 25 to 30 drops per minute. The dose was reduced when it was apparent that the infection was well controlled. Surgery was withheld whenever possible and was usually limited to incision and drainage of large abscesses developing in neglected or misdiagnosed cases. If small abscesses developed, their contents were aspirated with a syringe and needle, and the abscess cavity was partially refilled every two or more days with a solution of penicillin in physiological saline containing 5,000 units per cubic centimeter.

The clinical response to treatment and the roentgenological changes in the involved bones which developed subsequently were carefully observed.

RESULTS

Under the therapy outlined, all cases recovered but one of severe and neglected acute hematogenous osteomyelitis of the tibia with staphylococcus pneumonia and bacteriemia which was admitted in moribund condition and died seventeen hours later. The mortality rate was therefore remarkably low, being only 1.9 per cent. There was also a striking reduction of the period of morbidity.

The clinical results obtained fell into four groups and varied with the duration of the disease, the onset and adequacy of penicillin therapy, and the severity of the infection.

Group I. If the correct diagnosis was made early, within the first two or three days, and adequate treatment was started immediately, the results were truly excellent (example: Case 17). After a period of approximately thirty-six to seventy-two hours the fever, rapid pulse, bacteriemia, and other general signs of the severe infection began to disappear. At the end of a week, the temperature was usually normal, and the patient looked and felt quite well. The local signs of infection such as tenderness, edema, and redness also began to recede after a similar latent period of thirty-six or more hours. In this group immobilization by means of a plaster cast seemed to be of comparatively little importance, and there was an early return of function. In fact, it was practically impossible to keep some of the children off of the involved extremities as early as two weeks after the beginning of treatment. Surgical intervention was not necessary in this group unless an abscess formed.

The bony changes as depicted on the roentgenograms were minimal, consisting of areas of localized periosteal reaction, small areas of patchy decalcification of the underlying cortex, little or no evidence of sequestration, and ultimate reconstitution of the bone. These findings were hard to see in some instances and were temporarily overlooked at times. An additional 3 cases with typical symptoms and signs of acute osteomyelitis which were treated successfully with penicillin were not included in the report since it was impossible to prove the diagnosis in the absence of roentgenographic findings.

CASE 17. B. S., female, aged four, was admitted to Children's Hospital on June 5, 1944, complaining of severe pain in the right leg and high fever of two days' duration. Two weeks before, she had developed a blister on her heel which had become infected.

Examination showed a severely ill white child with marked swelling, tenderness and local heat above and below the right knee. On the right heel an infected superficial ulceration was healing satisfactorily. The white blood count was 16,500 cells per cubic millimeter with 79 per cent polymorphonuclear leukocytes.

The blood culture was positive for the hemolytic *Staphylococcus aureus* on June 5 and 7, 1944.

Roentgenograms (Fig. 1) taken at the time of admission showed no evidence of osteomyelitis. A clinical diagnosis of acute hematogenous osteomyelitis of the tibia and femur was made. The patient was placed on parenteral penicillin therapy giving 15,000 units every three hours at the beginning of treatment and 10,000 units at the same interval later. A small fluctuant area developed over the upper end of the tibia and this was aspirated on June 11, 1944. Thin, watery pus containing the hemolytic *Staphylococcus aureus* was obtained. Two days later this abscess was incised, liberating the purulent material and the leg was immobilized in a plaster cast. The patient's condition improved rapidly thereafter. During the course of illness two transfusions were given and a new cast was applied on July 26, 1944. Roentgenograms two months later showed thickening of the periosteum over the lower third of the right femur and upper third of the right tibia, with a small area of demineralization of the tibia just below the epiphyseal line (Fig. 1). Five months after the onset of the disease, roentgenograms showed practically complete healing of the bone. Her general condition was very good and she had no symptoms or signs of residual bony infection. Her clinical recovery was excellent and the bony damage minimal. In the light of our later experiences, incision and drainage of this small abscess was probably unnecessary.

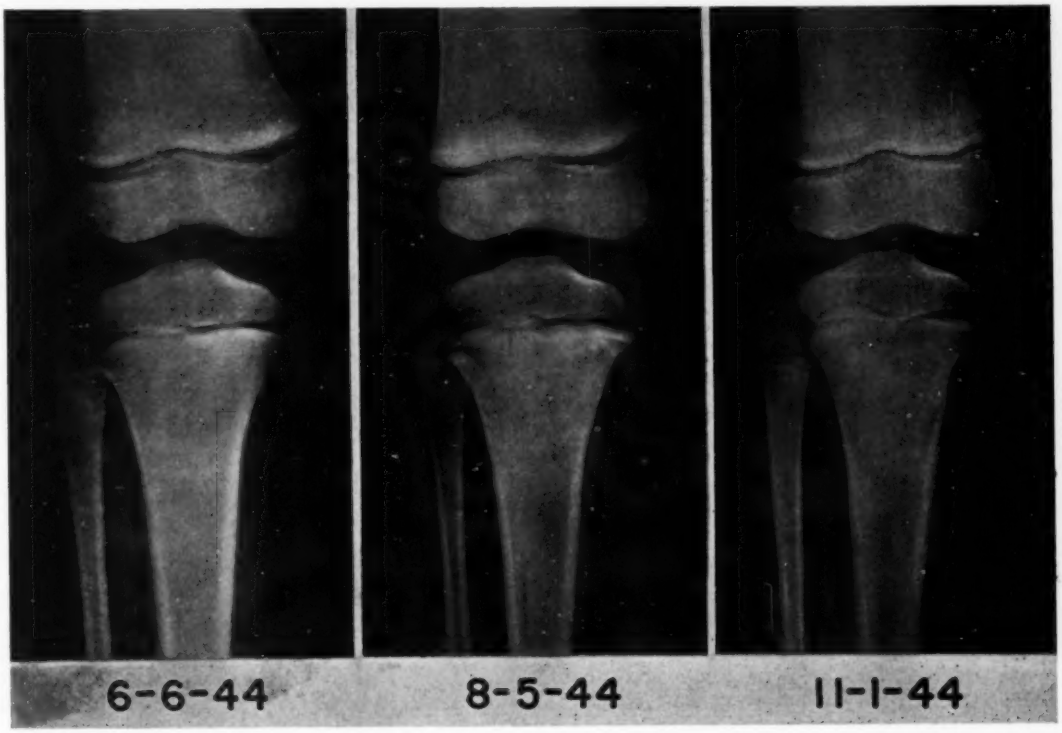

Fig. 1. Showing the bony changes occurring in Case 17. 6-6-44. No evidence of osteomyelitis or periostitis. 8-5-44. Considerable periosteal elevation, upper third of tibia. Mottling of bone just below epiphyseal line due to early bone involvement. 11-1-44. Practically complete healing of periosteum. Cortical infection at upper end has healed. No break has occurred in the cortex and no sequestration has taken place.

Group II. When the diagnosis and treatment with penicillin were moderately delayed, the general and local infections were brought under control less promptly after a period of two, three or more days during which little or no clinical response was evident. In this group local soft tissue abscesses developed more frequently. When small, they were treated successfully by aspiration of their contents and local injection of a solution containing 5,000 units

of penicillin per cubic centimeter at intervals of two or more days. If the abscesses were large, surgical drainage by incision was done to liberate the accumulated necrotizing bacterial toxins and to minimize further tissue destruction. When surgical drainage was carried out for large abscesses, the fall in temperature was usually prompt and not delayed for thirty-six or more hours as in the cases treated without surgical drainage.

The bony changes developing in these cases were of great interest. Usually none was visible on the roentgenograms at the beginning of treatment. After a week or more had elapsed, periosteal reaction and localized patchy demineralization of the underlying bone became evident and increased progressively in extent and degree, becoming most marked one to five months after the onset of the infection. Recalcification of the demineralized areas followed with re-establishment of a normal or nearly normal appearance of the bone. Sequestration did occasionally occur in this group.

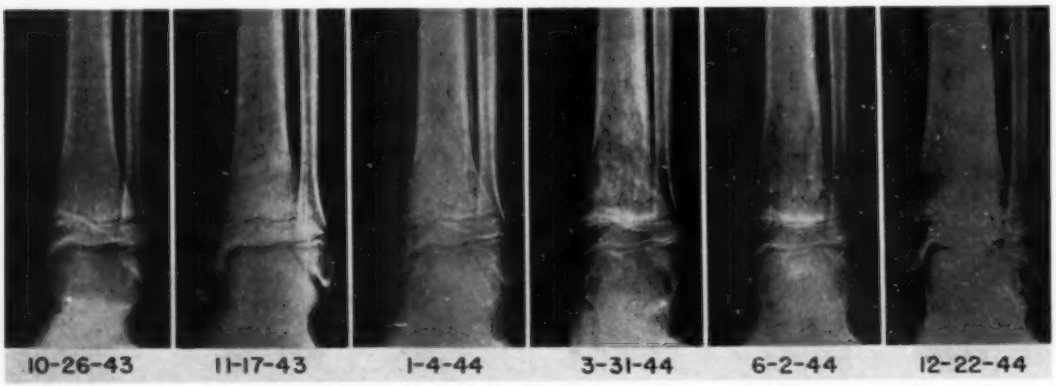

FIG. 2. Showing bony changes occurring in Case 4. 10-26-43. Small area of rarefaction on the outer aspect of tibia, just above the ankle, with a very tiny break in the cortex. No periosteal reaction on medial aspect, lower third. 11-17-43. Mottling of lower one-fourth of tibia due to irregular areas of rarefaction. Very slight periosteal reaction on medial aspect, lower third. 1-4-44. Mottling has increased in lower portion of tibia and periosteal reaction is now very well defined. Also slight periosteal elevation on outer aspect of fibula, distal one-fourth. 3-31-44. More extensive bone rarefaction and periosteal reaction than on previous roentgenograms. Several breaks in tibial cortex now easily seen. 6-2-44. Less mottling than previously and almost complete disappearance of the periosteal reaction. No sequestration anywhere. 12-22-44. All mottling has disappeared and no periosteal reaction remains. Healing of the infection appears complete.

CASE 4. K. M., white male, aged thirteen, was admitted to the Children's Hospital on October 26, 1943, complaining of pain in the left ankle and right knee of four days' duration. A furuncle had been present on the left elbow for one week, and five days before admission he had turned his left ankle while playing. The following day he had a shaking chill followed by fever and malaise and painful swelling of the left ankle occurred on the following day. Twenty-four hours later the same changes appeared in the right knee.

Examination showed an acutely and severely ill boy whose temperature was 102.5° F., pulse 130, and respirations 48. A large furuncle was present on the left elbow and numerous petechiae covered the trunk and extremities. Many râles were heard throughout both lungs, and the mucous membrane and nail beds were cyanotic. There was increased heat, marked swelling and exquisite tenderness about the left ankle and the lower half of the left leg. Limitation of motion of the right knee with swelling and tenderness over the lower medial aspect of the right thigh was present.

The red blood count was 4,300,000 cells per cubic millimeter and the white blood count was 11,750 cells with 79 per cent polymorphonuclear leukocytes. Urinalysis showed the presence of acetone and a trace of albumin. Blood cultures were repeatedly positive for the hemolytic *Staphylococcus aureus*. Roentgeno-

grams showed a small area of rarefaction of the outer aspect of the tibia just above the epiphyseal line with a very small break in the adjacent cortex (Fig. 2). Changes in both upper lung fields suggested an acute embolic pneumonitis.

A diagnosis of *Staphylococcus aureus* bacteriemia with acute hematogenous osteomyelitis of the right femur and left tibia and embolic staphylococcus pneumonia was made. Penicillin was started on the first hospital day and after two doses of 25,000 units he was given 15,000 units intravenously every three hours. Three and one-half days later the dose was reduced to 10,000 units and four days later to 5,000 units. It was discontinued on the twelfth hospital day. Both legs were supported in long casts which were bivalved for purposes of observation of the involved areas. Little response to penicillin therapy was evident for seventy-two hours, the temperature remaining high, the blood cultures remaining positive and the signs of local inflammation persisting. Following this, the fever gradually fell and reached 99° F. on the twelfth day after the start of penicillin therapy where it remained until the twenty-seventh hospital day.

On November 17, 1944, the roentgenograms showed periosteal elevation along the medial aspect of the distal end of the right femur and the lower third of the left tibia with mottling of the lower metaphysis of the tibia (Fig. 2).

He was discharged from the hospital on November 24, 1943, his thirtieth hospital day with no clinical evidence of active infection.

On January 4, 1944, the periosteal reaction was more marked on the tibia and evident over the outer aspect of lower end of the fibula. The mottling in the lower portion of the tibia had increased in extent and degree.

The casts were removed the first week in March and he was allowed to resume activity gradually. On March 31, 1944, there was more extensive rarefaction and periosteal reaction of the lower ends of the tibia and fibula than on the previous roentgenograms. Several breaks in the tibial cortex were easily seen. On June 2, 1944, partial recalcification of the areas of rarefaction and almost complete disappearance of the periosteal reaction indicated that healing was taking place. The last roentgenograms on December 22, 1944, were interpreted as showing further calcification of the previously rarefied areas with apparently complete healing. The clinical examination at that time showed no abnormality or evidence of active infection.

Case 3. J. C., white male infant, aged thirteen months, was admitted to Children's Hospital on October 23, 1943, with a history of fever associated with redness, swelling, and marked pain of the entire left lower leg of more than three days' duration. He had been given sulfathiazole without obvious clinical improvement during the three days prior to admission.

At the time of admission there were marked edema, redness and tenderness over the external malleolus, shaft of the fibula, and lower end of the tibia. The temperature was 102° F. and the white blood count was 32,000 cells per cubic millimeter. Urinalysis was essentially negative except for the presence of acetone. Blood cultures were negative. Roentgenograms showed no evidence of osteomyelitis. A clinical diagnosis of acute hematogenous osteomyelitis of the fibula was made. He was treated conservatively by immobilization of the extremity and administration of penicillin giving 15,000 units and later 10,000 units every three hours intravenously and intramuscularly. No surgical drainage was carried out.

Eight days after the onset of symptoms the cast was bivalved and a small subperiosteal abscess was aspirated yielding 12 cc. of thick gray pus containing staphylococci. The cast was reapplied and the patient continued to receive penicillin and general supportive therapy. On the fifth day after the start of penicillin therapy, the temperature began to fall, reaching normal six days later. The patient was discharged to his home with no external signs of active inflammation present in the leg. No draining sinuses or residual edema were apparent. Progress roentgenograms taken at intervals during the eleven months after onset of disease are shown in Figure 3.

On November 25, 1945, one month after admission to the hospital and approximately two weeks after completion of the penicillin therapy, considerable involvement of the proximal and distal ends of the fibula had developed with periosteal reaction involving most of the shaft and sequestration of practically two-thirds of the fibular shaft. Approximately three months after admission, on January 18, 1944, the periosteal reaction was increased in amount and was forming a new bony shaft for the fibula. The sequestrum of the old shaft of the fibula had been partially and spontaneously absorbed.

After this, the child moved to another state and contact was maintained through his

orthopedic surgeon. Shortly after moving, he developed two small draining sinuses in the lower part of the affected leg and the roentgenograms on April 29, 1944, showed that the long narrow sequestrum was detached and was working its way to the surface. During a subsequent change in plaster casts, the sequestrum was found to be partially extruded from one of the sinuses and was therefore removed. Approximately eleven months after onset of the disease, the roentgenograms showed reconstruction of the entire fibula with apparently complete healing. There has been no disturbance of growth of this leg, no deformity, and no impairments of function of adjacent joints. In October, 1944, the child was reported to be running about normally without complaints or signs of infection.

Group III. When the diagnosis and treatment were delayed for seven to ten or more days, or when the infection was unusually severe, local destruction of bone became very great and soft tissue abscess formation and sequestration occurred in most but not all of the cases. Sequestration, however, was usually of limited extent and in some cases the sequestrum acted as an autogenous bone graft, becoming revascularized and viable to participate in the reconstruction of the involved bone (Fig. 4).

The local infection was arrested with more difficulty in this type of case and longer periods of treatment with penicillin were usually required. Small abscesses were treated by aspiration and large ones by incision and drainage.

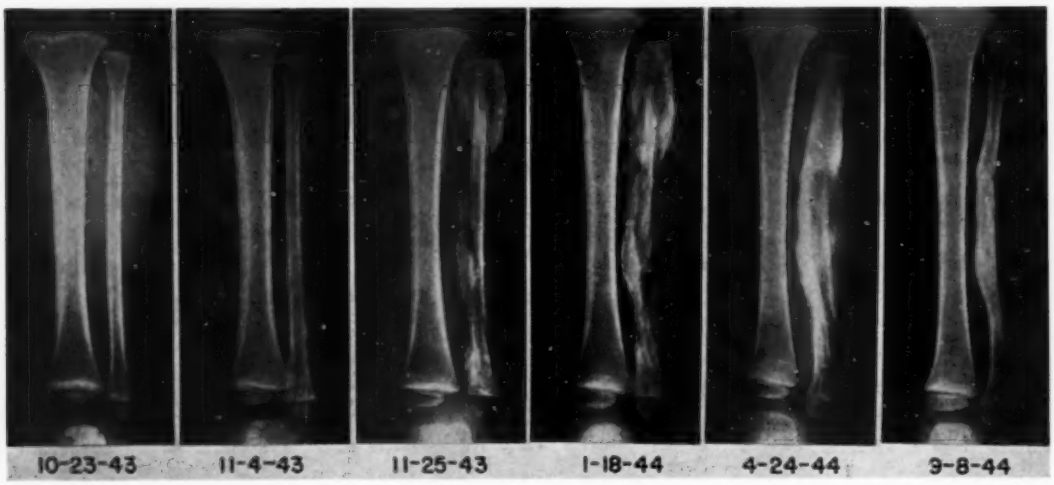

FIG. 3. Showing the bony changes occurring in Case 3. 10-23-43. No definite roentgen findings in bone or periosteum. 11-4-43. Rarefaction at proximal and distal ends of fibula with associated periosteal reaction. Also an area of periosteal reaction at level of junction of middle and lower thirds. 11-25-43. Bone destruction involving lower two-thirds of fibula. Absorption of proximal end. Marked periosteal reaction in these areas. Practically two-thirds of shaft is sequestrating. 1-18-44. Reconstruction has taken place in major portion of the fibula. The sequestrum is absorbing. Slight increase in the degree of periosteal reaction at proximal end. 4-24-44. Almost entire shaft has become recanalized. Long narrow sequestrum remains on outer portion of fibula in its middle third. 9-8-44. Entire fibula has been reconstructed. Remainder of sequestrum not absorbed has been removed.

The bony changes as revealed by roentgenograms showed extensive bone destruction at the start of penicillin treatment, which increased on subsequent examinations. Sequestration occurred in some instances. Smaller sequestra have been absorbed spontaneously and larger ones apparently have acted as autogenous grafts. In Case 3 the sequestrum was spontaneously and partially discharged while in Case 22, the large sequestrum is undisturbed, apparently viable and taking part in reconstruction of the shaft of the radius.

Case 21. R. S., white male, aged eight, was admitted on the pediatric service of the Cincinnati General Hospital on March 27, 1944, complaining of fever and a painful swelling in the left shoulder and elbow of four days' duration. Several days previously he had had a tonsillectomy.

On examination his temperature was 103° F., pulse 120, and respirations 26. The sclerae were icteric. There was a loud systolic murmur audible over the apex of the precordium. Extending from the left shoulder to the elbow was a hot, reddened, edematous area which was exquisitely tender. Limitation of motion of both elbow and shoulder joints was present.

The white blood count was 18,700 cells per cubic millimeter with 80 per cent polymorphonuclear leukocytes. The urinalysis was negative. The icteric index was 13 and cephalin flocculation test was 4+ in twenty-four hours. The van den Bergh test showed a moderately positive prompt biphasic reaction. Blood cultures taken then and subsequently were reported as negative and chest roentgenograms were essentially normal.

A diagnosis of rheumatic fever was made and treatment with antipyretics was started. Sulfadiazine therapy was started on March 31, 1944, the fourth day after admission, giving 1 gram every four hours without noticeable clinical improvement. On March 31 the roentgenologist described periosteal reaction about the upper two-thirds of the shaft of the humerus with some demineralization of the underlying bone (Fig. 4). Repeated roentgen examinations showed gradual increase in these changes which were quite extensive on the thirteenth hospital day. Pus was aspirated from a soft tissue abscess over the upper lateral aspect of the arm and the hemolytic streptococcus was cultured from it. At this time we were asked to see the patient, and it was elected to treat the osteomyelitic process with penicillin, giving 10,000 units every three hours intramuscularly. The soft tissue abscess was again aspirated and 15,000 units of penicillin in 3 cc. of saline

Fig. 4. Illustrating the bony changes occurring in Case 21. 3-31-44. Mottling at upper end of shaft of humerus and very slight periosteal reaction on outer aspect of upper one-fourth of shaft. 4-8-44. Mottling has continued down the shaft to junction of upper and middle thirds. Periosteal reaction present both sides of shaft. 4-18-44. Marked increase in periosteal reaction. Very small sequestrum seen under periosteum on outer aspect. 4-27-44. Osteomyelitis has increased considerably and a long narrow sequestrum is present on lateral aspect of shaft. Periosteal reaction has increased, particularly over the sequestrum. 6-22-44. Reconstruction of the shaft has taken place. The sequestrum has been involved in the process of recalcification and healing. 1-19-45. Complete healing and reconstruction.

solution were instilled into the abscess cavity. Within seventy-two hours after the penicillin was started, the temperature fell to 99.2° F., and thereafter this elevation was never exceeded. The subperiosteal abscess was aspirated on two occasions followed by instillation of penicillin. No organism was cultured from the aspirated material after eight days of penicillin therapy. The dose was reduced to 5,000 units every three hours after the eleventh day of penicillin treatment and discontinued two days later.

Serial roentgenograms of the involved humerus revealed striking bony changes (Fig. 4). On April 8, 1944, at the start of penicillin therapy, extensive destruction of the bone produced by the infection of thirteen days' duration was evident. Near the completion of penicillin therapy, the roentgenograms showed a marked increase in the extent of periosteal reaction and the formation of a small sequestrum. On April 27, 1944, one month after his admission to the hospital, the rarefaction of the humeral shaft and periosteal reaction had reached its maximum and a long narrow sequestrum was present on the lateral aspect of the shaft. Two months later (June 22, 1944) marked recalcification and reconstruction of the involved bone had occurred spontaneously, the sequestrum apparently participating in the healing process (Fig. 4).

He was transferred to the Children's Convalescent Home on his forty-seventh hospital day and an early return to normal activity was possible under supervision. After a stay of three months at the institution he returned home entirely without symptoms. Progress roentgenograms on January 19, 1945, showed apparently complete healing.

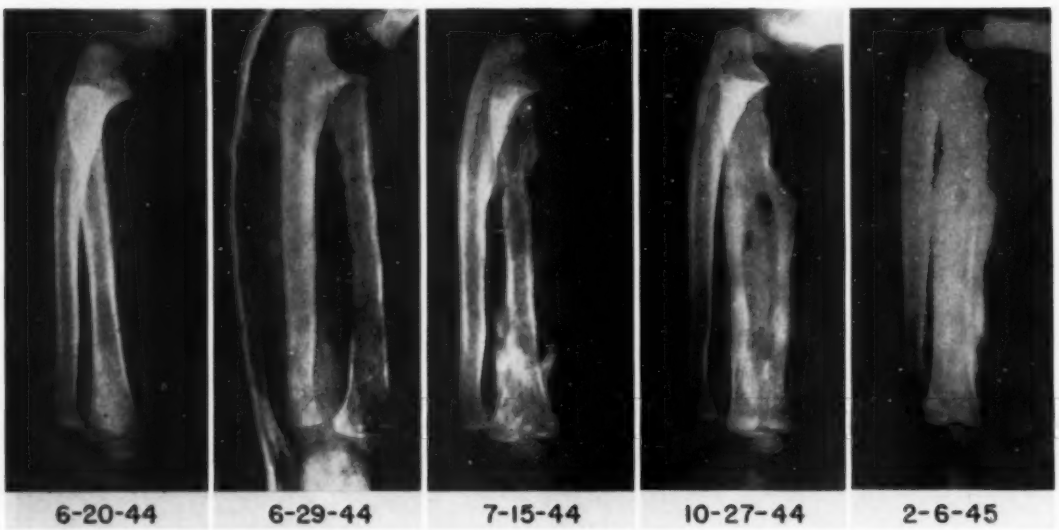

FIG. 5. Showing bony changes occurring in Case 22. 6-20-44. Rarefaction at distal end of radius, most likely early osteomyelitis. 6-29-44. Rarefaction has extended upward through distal half of radius and also involves the proximal one-fourth. Several breaks in the cortex. Periosteal reaction present, especially proximal end. 7-15-44. Very extensive periosteal reaction with absorption of both ends of the shaft and beginning sequestration of the middle third. 10-27-44. Extensive healing and reconstruction of the radius. The sequestrum representing the middle third of the radial shaft apparently has become revitalized. 2-6-45. Practically complete reconstruction of the radius.

CASE 22. R. J., Negro male, aged three, was admitted to the Cincinnati General Hospital on June 14, 1944, with a chief complaint of swelling throughout the right forearm. Two days earlier he had cut his right palm and at that time it was noted that he also had a furuncle of his scalp.

He appeared acutely ill and his temperature was 104.6° F. There was a healing laceration of the left thenar eminence. Extending from the left wrist to the shoulder was a warm, exquisitely tender swelling which was greatest throughout the forearm.

The white blood count was 21,000 cells per cubic millimeter and the urinalysis showed the presence of acetone. Blood cultures were reported as negative on admission as well as on repeated subsequent examinations. Roentgenograms on his sixth hospital day showed small areas of demineralization and periosteal reaction about the distal end of the radius, but these were overlooked.

A diagnosis of acute cellulitis of the forearm secondary to an infected laceration of the hand was made. Sulfadiazine was started, 7½ grains being given every four hours. Massive wet compresses were applied to the arm. After twenty days on sulfadiazine therapy he continued to have daily elevations of temperature to approximately 100° F. and the appearance of the arm did not change appreciably. The bone changes as revealed by the roentgenogram had progressed markedly. Rarefaction of the distal half and proximal fourth of the radius with periosteal reaction was obvious, and several breaks in the cortex became visible, making the diagnosis of acute osteomyelitis of the radius apparent.

On the twenty-third hospital day, we were asked to see the patient and pencillin therapy was started, giving 10,000 units intramuscularly every three hours. Sulfadiazine was discontinued. The arm was immobilized in a long arm cast. After five days the dose was reduced to 5,000 units every three hours. The course was one of slow improvement. The roentgenogram taken on July 15, 1944, showed more extensive periosteal reaction with absorption of both ends of the radial shaft and beginning sequestration (Fig. 5). On July 20, 1944, after fourteen days of penicillin therapy, aspiration of the forearm yielded a few cubic centimeters of fluid from which hemolytic *Staphlococcus aureus*, *Staphylococcus albus*, and a streptococcus were cultured. He was discharged on his fifty-sixth hospital day greatly improved. When seen in the clinic on August 28, 1944, there was still some swelling of the forearm with a palpable irregularity along the surface of the radius. Progress roentgenograms taken on October 27, 1944, 137 days after the onset of illness, showed that the periosteal reaction had thrown up an enveloping bridge of new bone about the sequestrum representing the old radial shaft. Of particular note is the apparent revitalization of the sequestrum similar to that seen in autogenous bone grafts. On February 6, 1945, 239 days after the onset of the disease, marked healing had occurred with recalcification and spontaneous reconstruction of the radius. The sequestrum had participated in this process.

Group IV. In certain fulminating infections in which it is apparent that the patient will not live the forty-eight or more hours necessary to obtain the maximum effect of penicillin, surgical intervention after adequate preoperative preparation is still necessary as an emergency measure. Penicillin was administered preoperatively and postoperatively in doses of at least 15,000 units every one to three hours. In such instances, the bone destruction was extensive due to the severity of the infection.

Case 29. G. C. white male, aged two, was admitted to the Children's Hospital on July 6, 1944, complaining of pain and swelling of the left foot and lower leg of three days' duration. Wet dressings had been applied and an unknown type of sulfonamide administered the day before admission. During the preceding two weeks he had an acute upper respiratory infection and ten weeks before he had had epidemic meningitis from which he had made a complete recovery.

Examination showed an acutely ill and profoundly toxic white boy whose temperature was 104.2° F. There was a profuse nasal discharge. The left foot was red, hot, tender, and swollen to a level about the ankle. A large vesicle containing blood-stained fluid was present over the area of greatest swelling.

The white blood count was 15,250 cells with 86 per cent polymorphonuclear leukocytes and the red blood count was 3,960,000. Urinalysis showed the presence of albumin and an occasional red blood cell. All blood cultures taken were negative. Roentgenograms on July 7, 1944, showed swelling in the soft tissues, but unfortunately they showed only a small portion of the lower leg (Fig. 6).

Aspiration of the fluid in the large hemorrhagic vesicle was performed and examination of a stained smear of this material showed the presence of numerous small chained gram-positive cocci. These were interpreted as streptococci and a tentative diagnosis of hemolytic streptococcic gangrene was made.

Sulfadiazine gr. v and an equal amount of bicarbonate of soda were given every four hours. Penicillin was started on the second hospital day, 10,000 units being given intramuscularly every three hours to an infant of two years of age.

The patient's condition became rapidly worse during the ensuing twenty-four hours, and it became evident that he would die before the passing of an additional twenty-four hours. At this time it was learned that the culture dorsum of the foot. On the lower lateral aspect of the leg an area of slough with perforation was found in the fascia. The wound was loosely packed with gauze incorporating four Dakin's tubes and the patient was returned to his room in very poor condition. He received continuous oxygen therapy, intravenous injection of 5 per cent glucose in saline solution, and several transfusions of 250 cc. of fresh whole blood. Treatment with penicillin was continued giving 15,000 units every three hours for the next

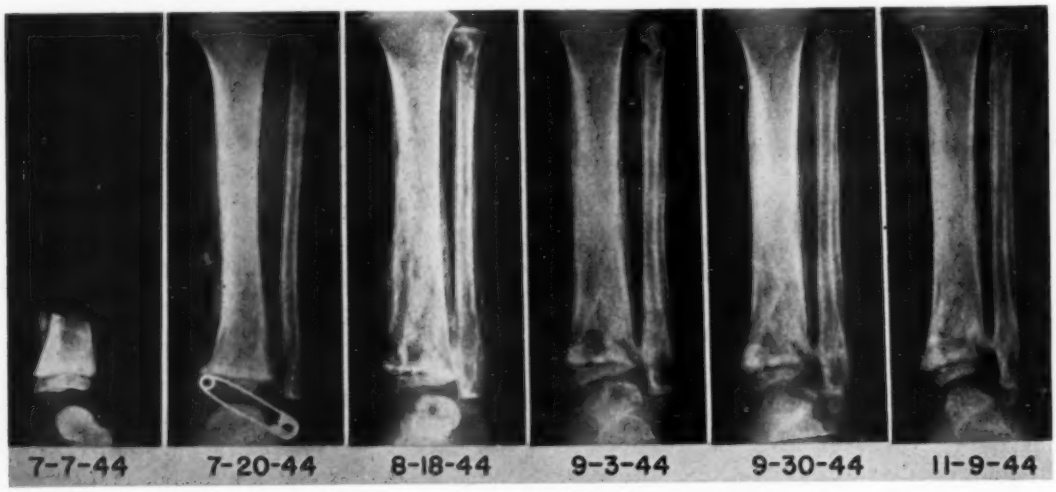

FIG. 6. Illustrating bony changes occurring in Case 29. 7-7-44. No evidence of bone or periosteal involvement. 7-20-44. Area of bone destruction at both ends of fibula and an area of rarefaction with break in cortex on medial aspect of distal end of tibia. Periosteal elevation on lateral aspect of tibia, distal half. 8-18-44. Extensive destruction both ends of fibula and lower half of tibia. Periosteal reaction has developed along the full length of both shafts. 9-3-44. Progress of the infection has been halted and healing has begun, both in the bone tissue and the periosteum. 9-30-44. Both ends of fibula and lower end of tibia have become recanalized. The tibial periosteal reaction of the periosteum of the fibula is about the same. 11-9-44. Reconstruction of upper end of fibula is complete. Deformity at lower ends of fibula and tibia has persisted but the infection has apparently completely subsided. Tibial periosteum has returned to normal except for a small area on medial aspect of shaft. Periosteum of fibula remains thickened.

of the fluid aspirated from the vesicle showed that the gram-positive coccus was a hemolytic *Staphylococcus aureus*, and not a hemolytic streptococcus. A diagnosis of acute hematogenous osteomyelitis was made and immediate operative intervention was decided upon. On the way to and in the operating room the child had two series of generalized convulsions. Under drop ether anesthesia two long incisions were made rapidly through the skin and subcutaneous tissues of the lateral and medial aspects of the leg and foot. A necrotizing purulent infection was found in the subcutaneous tissues over the entire leg and eighteen days and 10,000 units at the same interval for an additional eight days.

Striking improvement occurred in his general condition, becoming evident within the first twenty-four hours after operation and continuing during the following seven days. The sloughing tissues in the wound were replaced by red healthy granulation tissue and the wound gradually and spontaneously healed with the exception of a small area 2 cm. in diamater over the lower lateral aspect of the leg.

Roentgenograms taken on July 20, 1944, twelve days after onset of penicillin therapy

and ten days after operation, showed destruction and periosteal reaction at the distal ends of the tibia and fibula and involvement of the tibio-astragalar joint. A long leg cast was applied on the twenty-first day after operation and he was discharged on the forty-seventh day. He was afebrile at this time and his general condition was very good. On August 18, 1944, forty-one days after start of penicillin, and after its completion, the appearance of the roentgenograms was much worse than it was at any time before or during the administration of penicillin. Extensive demineralization and rarefaction of both ends of the fibula and lower half of the tibia with marked periosteal reaction along the full length of both shafts had developed. Fifty-seven days after the start of penicillin, early healing had become manifest by fusion of the periosteal new bone with the cortex and beginning recalcification of the rarefied areas. There was no evidence of sequestration. On November 9, 1944, 129 days after the onset of the illness, marked healing had occurred with complete reconstruction of the upper end of the fibula and tibia, and partial recalcification and reconstruction of the lower end of the tibia and fibula. In October, 1944, the patient began active weight bearing after removal of the cast. On November 23, 1944, the wound had completely healed and the patient was without complaint.

DISCUSSION

The roentgenographic changes in bone occurring in acute hematogenous osteomyelitis treated with penicillin are of particular interest. Early in the disease, during the first four to ten or more days, the roentgenograms are of no practical value in detecting the nature of the disease. This emphasizes the fact that the diagnosis of acute osteomyelitis is purely a clinical one at the time when early and adequate treatment with penicillin will minimize or prevent damage of bone. In many instances, penicillin therapy had sterilized the blood stream and had brought the generalized and localized manifestations of infection under control before any evidence of bone damage became obvious.

Later in the disease, usually after the cessation of chemotherapy, a succession of roentgenographic changes occurred. These changes varied with the age of the patient, the severity of infection, the duration of infection before treatment with penicillin, the adequacy of therapy, and the type of infecting bacteria. Periosteal reaction, patchy areas of demineralization and rarefaction of the involved bone, and breaks in the adjacent cortex were early signs which usually became evident ten to fourteen days after the onset of the illness. These findings increased in extent and degree, and were invariably interpreted by the roentgenologist as representative of "an extension of the osteomyelitic process." We have learned to interpret the areas of rarefaction and breaks in the cortex of the involved bone as a measure of spontaneous absorption of the bone destroyed early in the course of the infection rather than a measure of an extension of the osteomyelitic process. The process suggests that adequate penicillin therapy given early arrests and controls the infection, converting an area of septic necrosis of bone to one of aseptic necrosis.

The spontaneous absorption of the dead bone is followed by recalcification of the involved area often with re-establishment of normal or near normal bony architecture. Reconstitution of the bone was accomplished with less resultant bone sclerosis than that seen by other previous forms of treatment.

We suspect that a process similar to that seen following the transplantation of autogenous bone grafts occurs in acute osteomyelitis treated adequately with penicillin. It has been known for a long time that aseptic absorption of dead bone occurs in transplanted bone grafts.[2] When bone is transplanted to another location, a considerable part of it dies, but those bone cells which are still bathed in lymph and body fluids continue to live and show marked proliferation in the course of a few days. Revascularization of the necrosed bone is accomplished by new vessels growing from the surrounding tissues into the haversian canals. Proliferating osteoblasts accompany the new vessels, giant cells appear and the

dead bone undergoes absorption and conversion into a series of spaces lined by osteoblasts. The formation of new bone is then accomplished by these cells. In this manner the graft becomes partially absorbed and then replaced.

Although sequestration was relatively uncommon in cases treated with penicillin, it still occurred late in the illness if the infection was unusually severe, the diagnosis was delayed or the treatment inadequate. When it did occur, it was usually followed by spontaneous absorption of the smaller pieces, partial absorption of the larger ones, spontaneous extrusion of detached larger sequestra, or by recanalization and organization of large sequestra similar to autogenous bone grafts. Sequestrectomy may be necessary in 2 cases later.

In the past we have been impressed with the degree of secondary infection in areas of osteomyelitis treated by surgical drainage. Devitalized tissue exposed to the air invites mixed or saprophytic infection, particularly by various gram-negative bacilli, and it is often difficult to prevent this type of infection. Such secondary invaders have frequently been penicillin resistant or even penicillin destructive. The elimination of this complication by penicillin therapy may be a very important factor in the arrest of the local infective process and the spontaneous absorption of devitalized bone.

SUMMARY AND CONCLUSIONS

Penicillin is a powerful chemotherapeutic agent which has reduced the mortality and morbidity in acute hematogenous osteomyelitis by effectively bringing the infection under control and by decreasing the local destruction of bone and resultant deformities. A study of cases treated with penicillin has radically altered our interpretation of the roentgenographic changes developing in this disease. Although the roentgenogram is of little or no value in making an early diagnosis of acute hematogenous osteomyelitis, it is of definite value in the recognition of the process after ten to fifteen days beyond the onset. A succession of changes occurring in bone have been described in the cases treated adequately with penicillin which have been interpreted as a measure of the process of spontaneous repair and not as an indication of further extension of the osteomyelitic process as has been generally assumed. The spontaneous removal of necrosed bone has been followed by recalcification and healing of the involved areas.

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Vol. 54, No. 5

STUDIES ON ROENTGEN DEATH IN MICE*

I. SURVIVAL TIME AND DOSAGE

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INTRODUCTION

THE series of investigations of which this is the first report deals with reactions of mice to lethal doses of roentgen rays. The emphasis will be on reactions which can be measured, on their quantitative relations to the doses administered, and on the evaluation of factors which influence the dose-response relation. The present paper deals with the speed of the processes leading to death expressed by the survival time elapsing between irradiation and death. The dosage range investigated extends from 500 to 25,000 roentgens. It will be shown that it is divided into four zones, each with distinctive characteristics of the dose-response relation.

MATERIAL

Inbred mice were used in these experiments. They were from five to twenty-five weeks old and weighed 20 gm. ± 15 per cent, i.e., from 17.4 to 23.0 gm. They were kept in wooden bins, 2 to 20 mice in a bin, and had unlimited access to water and food ("Purina" dog chow).

Our standard strain† is C57-Black. These mice are derived from a Bar Harbor strain, and have been continued in Illinois since 1938 by successive brother-to-sister matings. Some of the mice represented in this report come from two other strains of about equal roentgen sensitivity, called strains L and B. Strain L is derived from the Swiss stock, and has been inbred systematically in Illinois since 1939. Strain B is an anophthalmic strain, inbred since 1938 in Bar Harbor, and later in Illinois, and described in a series of papers by H. B. Chase and E. B. Chase.[1] In addition, a few first generation hybrids between the above strains were used.

METHOD OF IRRADIATION

The definition of the roentgen dose administered to a mouse involves certain difficulties. The biologic effect depends on the tissue, or effective, dose. This dose consists of two components, the primary radiation delivered, and the secondary radiation arising within the irradiated subject. The amount of the latter depends on the size and shape of the object. It is small if the beam of rays hits only a single mouse, becomes considerable when several mice are irradiated together in a box, and reaches up to 50 per cent of the primary radiation if the mice are subjected to backscatter from the support. Thus, the effective intensity can deviate considerably from the primary intensity.

In general it is desirable to know the absolute value of the effective dose. This can be accomplished in two ways: either by irradiating the mice singly, suspended free in air with a minimum of support, in which case the tissue dose is practically equal to the amount of primary radiation delivered; or, by arranging the mice in a way that the amount of secondary radiation they receive is measurable and reproducible. The latter way is the one we selected.

A phantom was designed to permit irradiation with doses which are reproducible, measurable, and nearly homogeneous throughout the body of the animals. It was built of sheets of pressdwood, sp. gr. 1.1, measuring 16 by 16 by $\frac{1}{4}$ inches. In the center of six sheets, rectangles of 2 by 3 inches were cut out; these sheets were bolted together with a seventh one which formed the bottom. A sheet placed on top of this block formed the ceiling of a chamber

† A strain is obtained by continued and uninterrupted brother-to-sister matings in successive generations. Mice belonging to one strain are the closest approach to genetically homogeneous mice which can be obtained. A stock is obtained by continuous inbreeding within the progeny of one couple, without regard to the relationship between mates. A stock is less pure than a strain.

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measuring 3 by 2 by 1½ inches, situated in the center. The whole block was placed on fifteen additional sheets of pressdwood providing the backscatter. The central beam was directed through the center of the block. Two to 4 mice were irradiated at a time. They filled about half the space in the chamber. The remaining, irregularly shaped air space proved to be sufficient to prevent anoxemia and is not believed to change substantially the dose distribution.

It can be seen that the postulate of homogeneous dosage distribution was reasonably well fulfilled. The variety of settings used is due partly to changes in the apparatus (the experiments were carried out during a period of two years), partly to special investigations which yielded negative results, i.e., the differences between the settings described did not appreciably influence the effects obtained. Setting G involved the use of a special phantom designed

TABLE I

SETS OF IRRADIATION CONDITIONS USED

Setting	kv.* max.	Filter	Half-Value Layer in mm. Cu	ma.*	Distance Target-Center of Chamber in cm.	Effective† r/min.	Highest** r/min. in Per Cent of Effective r/min.	Lowest‡ r/min. in Per Cent of Effective r/min.
A	183	0.75 mm. Cu +1 mm. Al	1.20	6.25	52.5	15.4	102	97
B	200	0.75 mm. Cu +1 mm. Al	1.34	10.0	92.0	9.5	102	97
C	200	0.75 mm. Cu +1 mm. Al	1.34	10.0	48.75	18.8	102	97
D	200	0.75 mm. Cu +1 mm. Al	1.34	10.0	37.5	33.6	103	96
E	200	0.5 mm. Cu +1 mm. Al	1.10	8.0	37.5	37.6	104	94
F	200	None	0.34	8.0	37.5	117.0	106	93
G	200	None	0.34	8.0	27.0	220.0	—	—

* As read on the instruments on the control panel.
† Intensity at a point 1.5 cm. above the floor of the chamber and 2.5 cm. off center.
** Intensity at a point 0.5 cm. below the ceiling, in the center beam—considered the highest intensity likely to hit any sensitive part of the mouse.
‡ Intensity at a point 0.5 cm. in each direction from a lower corner of the chamber—considered the lowest intensity likely to hit any sensitive part of the mouse.

For the determination of depth dose distributions, the block of sheets with the chamber was replaced by another set of sheets containing a tunnel into which the thimble of a Victoreen condenser r-meter was introduced.

Figure 1 shows the mouse chamber and dosage distribution charts for two different sets of conditions (settings) used, one considered satisfactory, the other showing poorer homogeneity of dosage.

Table 1 contains the data for all of the settings used in the experiments here reported.

for high intensity with little regard for dose distribution. This phantom consists of a cylinder of pressdwood which contains a cylindrical chamber of 5 cm. diameter and 2 cm. depth. It was used only for the highest doses.

GENERAL OBSERVATIONS

Several descriptions of the clinical and pathological picture of roentgen death in mice and other mammals have been given lately.[2,4,5,6,7,8,10] We can therefore restrict this chapter to a brief survey.

(1) *The Hyperacute Reaction.* A hyperacute reaction is produced by doses of 8,000 r and more, in our standard mice (C57-Black of about 20 gm. weight). The clinical picture is dominated by convulsions which appear immediately after doses of 15,000 r and more, after a latency period of a few hours with doses of 8,000 r. The symptoms are light and transitory with doses up to 12,000 r. With higher doses, the convulsions become increasingly severe, and death occurs during an attack at from three days down to minutes after the irradiation.[6]

(2) *The Acute Reaction.* Acute roentgen death is produced in about three and one-third days by doses from 1,175 to 12,000 r. The earliest symptom we observed is weight loss, which can be found, in the majority of cases, almost immediately after the irradiation. The weight decreases steadily ,and reaches about two-thirds of its original value at the time of death. On the second to third day, anorexia and diarrhea,[8] pallor, and flurriness of the fur become manifest. On the third day, the animals become weak, move little and slowly, and show a characteristic arching of the back. An hour or so before death, the respiration begins to slow down, and death occurs usually with terminal convulsions.

Pathological examination reveals a multiplicity of marked changes in many vital organs such as liver, spleen, lungs, kidneys, and intestines. In some cases, every one of these organs seems to be damaged severely enough to account by itself for the death of the animal.[10]

Doses of 600 to 1,200 r produce always, doses from 300 to 600 r sometimes, the picture of acute roentgen death, with the only difference that the course is slower and the interval between irradiation and death lengthened up to two weeks.

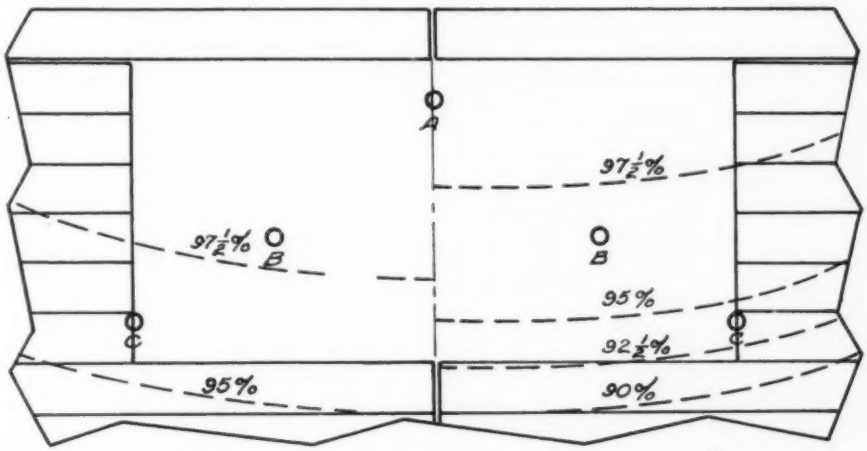

Fig. 1. Section through the mouse chamber of the phantom, with isodose lines for two settings. The effective intensity is measured at point *B*, the highest at *A*, the lowest at *C*.

(3) *The Subacute Reaction.* In the dosage range from 200 to 600 r, the weight, which first decreases, is sometimes arrested at a constant level for periods of days, or starts increasing again. This intermediate stage is sometimes followed by a second phase of more or less rapid weight loss accompanied by symptoms similar to those of the acute phase, and leading to death in one to six weeks after the irradiation.

The pathological picture is different from that observed in acute roentgen death. The spleen is often enlarged and shows intense regeneration of white cells. The liver is often enlarged, sometimes fatty. In some cases it shows zones of necrosis alternating with zones of healthy regenerating cells. Changes in the lungs are sometimes localized to a single lobe.

(4) *Survivors.* Animals surviving doses of 200 r and more, are sterile, grow less than their litter mates, and have a grizzly coat. Otherwise, they appear healthy. On pathological examination, the organs appear normal except for occasional fibrosis.

SURVIVAL TIME

The survival time is the time elapsed between irradiation and death. Our records of survival time and doses for 101 mice of about 20 gm. weight, which died within forty days after irradiation, are assembled in Figure 2. Each symbol represents an individual mouse, its position indicating the survival time (between irradiation and death) and the dose.

A certain margin of error is conceded for both the values of dose administered, and survival time. The dose estimate might differ from the actual dose delivered by up to 3 per cent because of fluctuations in the output of the machine. Another 3 per cent might be added for effects of position of the mice within the irradiation chamber. In addition, there is the possibility of gross errors in timing the irradiations. The survival time could be determined precisely in a few cases where the dying was actually observed. Most mice died at times when checks were being made at frequent intervals, so that in these cases the survival times are accurate within one-tenth of a day at the most. About one-fourth of the mice died at times when checks were being made at irregular intervals ranging up to twenty hours, and in these cases our estimate (based on the degree of postmortem changes present) may be off by up to one-fourth of a day.

The survival times of mice which have received a given dose show some variation, with

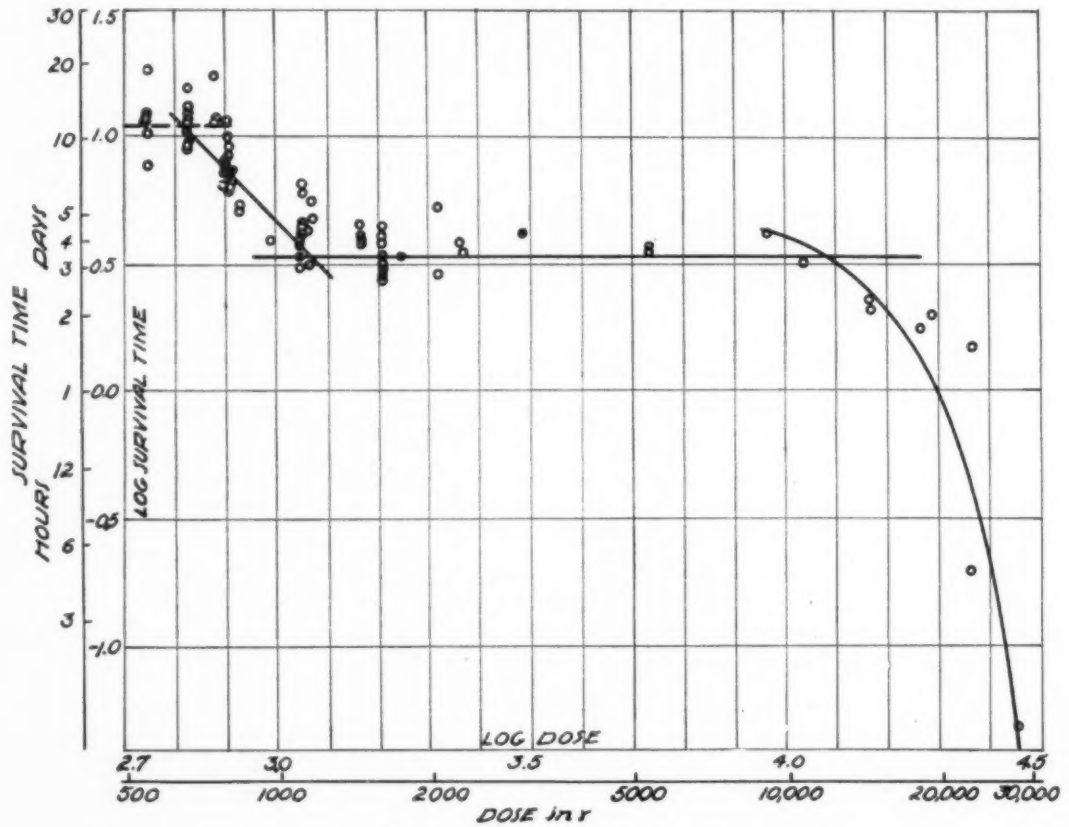

FIG. 2. Survival time of mice after whole body irradiation. Abscissa—dose in roentgens; ordinate—survival time in hours and days; circles—individual observations.

the longest intervals between irradiation and death about twice as long as the shortest intervals observed with the same dose. Some of this dispersion can be accounted for by experimental inaccuracies, but most is due to true variability. Hence, it is necessary to use statistics in order to obtain a simple expression of the dose-survival time relation. As a single value representing the class of survival times obtained with a given dose, we have selected the "logarithmic mean survival time," which is nearly identical with the "median survival time" (m.s.t.), i.e., the time after which 50 per cent of all observed fatalities have occurred. With doses which kill all the mice irradiated, the median survival time is identical with the time after which one-half of all the animals in the set have succumbed; but if, say, only 60 per cent die, the median survival time is the time after which 50 per cent of these 60 per cent, or 30 per cent of the total lot, are dead; and if only 6 out of 100 mice in a given set die, the median survival time lies between the occurrence of the third and the fourth fatality.

The trend of the median survival time, as estimated from the observations accumulated thus far, is represented by heavy lines in Figure 2. Full lines indicate the regions where we have enough material to feel that the present estimates will not be subjected to substantial corrections by further observations; dashed lines indicate a zone where the scarcity of experiments does not allow more than a preliminary estimate of the trend.

An inspection of the graph (Fig. 2) reveals that there are at least four different segments characterized by the form of the dose-response relation. The first segment, at the extreme left, seems to be a plateau, which represents survival times in subacute reactions. The few deaths observed in this low dosage range occurred after survival times of around eleven and one-fourth days.

The second and third segments represent survival times in acute reactions. The second segment extends over a dosage range from 650 to 1,175 r. It is sloping, indicating that in this zone the survival time decreases as the dosage increases. The third segment, which is the dominating feature of the whole curve, is a plateau extending over a domain of doses from 1,175 to 12,000 r. In this zone, the survival time remains at a fixed value, and changes in doses are ineffective as far as the survival time is concerned. That does not mean that changes of dosage, within this domain, will have no effect at all. For instance, motor symptoms appear at a dose of 8,000 r, and become progressively severe as the doses increase; but the survival time remains the same up to 12,000 r.

The last segment, to the right of the plateau, is the zone of the hyperacute reaction. The survival time decreases with increasing doses, first slowly, later rapidly.

It can be seen that the scattering of the symbols representing individual observations is most pronounced in the zones of transition between any two segments of the curve. It appears that in these zones of transition there may be an element of chance which determines in which of two ways an individual case may react.

In mathematical terms, the relation between dose administered (D) and median survival time (T) can be expressed as follows:

1.1 $\ldots T = \text{constant} = 11\frac{1}{4}$ days $\ldots (D < 750$ r)

1.2 $\ldots T.D = \text{constant} = 4.64 \times 10^6$
$\ldots (650 \text{ r} < D < 1{,}250 \text{ r})$

1.3 $\ldots T = \text{constant} = 3\frac{3}{4}$ days
$\ldots (1{,}000 \text{ r} < D < 12{,}000 \text{ r})$

1.4 $\ldots (\log T - 1.05) \times (\log D - 4.55) = \text{constant}$
$= 0.25 \quad \ldots (D > 10{,}000$ r)

The overlapping of the ranges of the four functions indicates the "uncertainty of reaction" observed in the transitional zones. At the present stage of investigation, the formulae given are only descriptive empirical approximations and should not be interpreted as statements of the form of relation between dose and effect.

DISCUSSION

The dose-response curve here presented is new if considered as a whole, but for every single zone there are corroborative data in the literature.

Several authors have investigated dosage ranges corresponding to the first and second segment of our curve. Sugiura[9] and Ellinger[2] have presented their data in a form which allowed the estimation of the median survival time. The results of these authors are entered in Figure 3, together with the curve we obtained. It is evident that the shape of the curve is about the same for all sets of data. The subacute plateau comes upper end of this plateau was not investigated, but presumably there are doses which kill goldfish more rapidly. In studies on mammals (mice and guinea pigs) Ellinger[2] failed to establish the presence of plateaus because he did not extend his investigations to high enough doses.

The picture of the hyperacute reaction is found in the early literature and has lately been described in detail by Henshaw.[4,5,6,7]

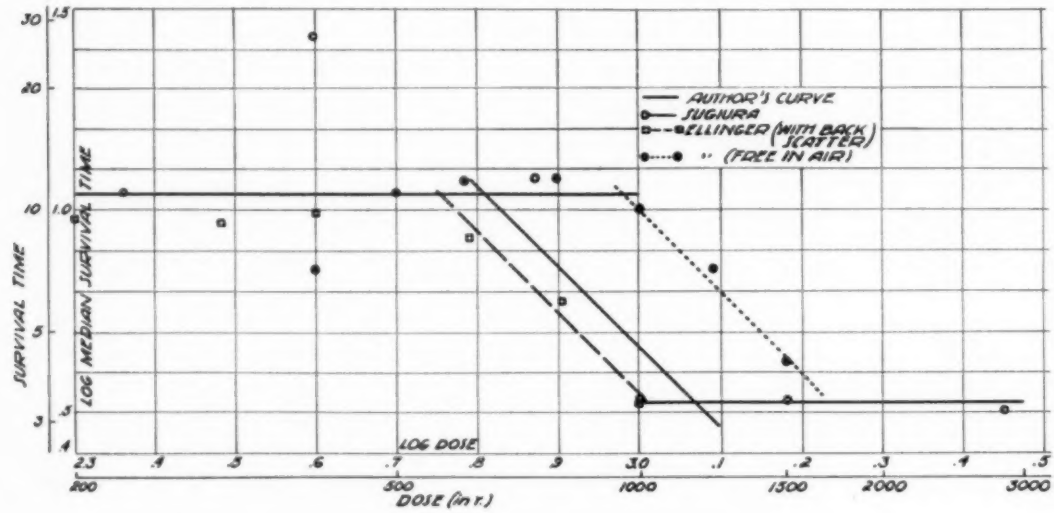

Fig. 3. Survival time and dosage. Author's curve, and data of Sugiura and Ellinger. Each symbol represents a class of mice.

out rather well in Ellinger's material. The position of the curves differs. Sugiura's data fit our curve. The two sets of Ellinger's data have been obtained with and without utilization of backscattering. From the curves, the amount of secondary radiation is estimated at 58 per cent which approximates the value of 50 per cent we would expect under the experimental conditions used.

A plateau has not been found in mice previously, but one presumably analogous to ours was established in goldfish by Ellinger.[3] Within a dosage range of from 200 to 2,000 r, increasing doses produce higher frequency and faster occurrence of deaths. At 2,000 r, the mortality is 100 per cent, and the median survival time about ten days. The reaction remains the same when the dosage is increased up to 10,000 r. The This author had worked with small and medium doses on mice, guinea pigs, and rabbits, and proceeded to investigate whether and how far the life span after irradiation could be shortened. He used huge doses, beyond the plateau range. On C3H mice, survival times of thirty-six to forty-eight, and twelve to twenty-four hours, respectively, were recorded after doses of 25,000 and 50,000 r. On subjecting the animals to radiation at a rate of 7,000 to 10,000 r per minute, death was observed in twenty-two minutes from the start of the experiment. Our own findings agree in general with Henshaw's, only we found the hyperacute reaction in a somewhat lower dosage range.

This short survey shows that each phase of the reaction has been studied before: the phases we call subacute, acute, and

hyperacute are all known. However, the segmental character of the dose-response relation has not been brought out, nor has the presence of the plateaus been established.

Histopathological studies have not gone very far to explain the mechanism of roentgen death. Several explanations have been offered; none has been generally accepted. Several tissues and organs show severe changes, and have, in turn, been considered as the decisive factor. We do not believe that pathological findings can resolve this conflict of opinion.[4,5,6,7,8,10]

The segmentation of the dose-response curve suggests that there is more than one mechanism involved in roentgen death. A very simple explanation of the segmentation of the curve is that there are three separate reactions. A first reaction has a maximum response corresponding to the subacute plateau; a second reaction has a threshold at 600 r and a maximum response at three and one-third days, corresponding to the acute plateau; a third reaction has a threshold around 8,000 r and a response which is not bounded by a maximum value.

Observations other than survival times support the idea of distinct mechanisms corresponding to the three phases. Subacute and acute reactions are differentiated by the weight curve which is biphasic in the former, monotone in the latter, and by the pathological picture; acute and hyperacute reactions are differentiated by the motor symptoms.

Our observations have not disclosed any specific information about the mechanism of roentgen death. They have strongly suggested that more than one mechanism is involved, different reactions dominating in different dosage ranges. It seems, however, that their number is limited, probably to three. Thus it can be hoped that the problem, while certainly not simple, is not exceedingly complex.

SUMMARY

1. Mice of 20 gm. weight were irradiated with roentgen rays. The doses ranged from 500 to 25,000 r. The tissue doses were about homogeneous throughout the whole body.

2. The reactions produced are classified as subacute, acute, and hyperacute reactions.

3. The survival time (between irradiation and death) is used as a quantitative measure of the irradiation effect. To characterize the reaction of a whole class of mice we use the mean logarithmic survival time, or the almost identical median survival time, i.e., the time after which one-half of all fatalities have occurred.

4. The relation between survival time and dose administered shows four zones with distinctive dose-response characteristics. There are two zones where the survival time decreases with increasing dose, and two plateaus where the survival time remains constant over considerable dosage ranges.

5. Simple mathematical formulae for the survival time-dosage relations are given.

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STUDIES ON ROENTGEN DEATH IN MICE*

II. BODY WEIGHT AND SENSITIVITY

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INTRODUCTION

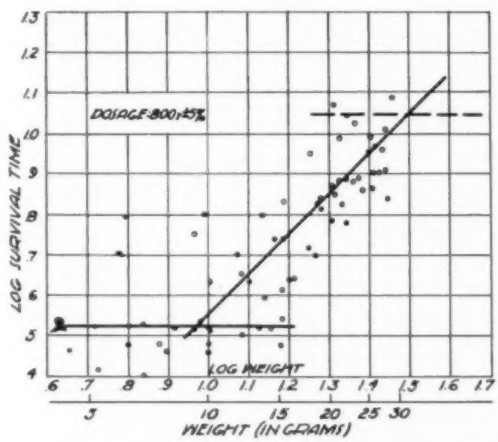
IN THE first paper[2] of this series, the relation between roentgen dose administered and survival time was established for mice of a standard weight. In the present, the second paper, the discussion will be extended to mice of various weights. It will be shown that the reactions which occur in mice of different weight are identical, but that the doses necessary to elicit a given response vary with the weight. Thus, the body weight is a factor determining the sensitivity to roentgen rays. In terms of the graph, a change of body weight causes the whole dose-response curve to shift parallel to the dosage axis.

C57-Black mice were used for this investigation. The methods of irradiation and observation were the same as described in the preceding paper.[2]

EFFECTS OF CONSTANT DOSES ON MICE OF VARYING WEIGHT

The effect of weight on survival time was studied on sixty-seven C57-Black mice, aged twenty-five days or more, which were subjected to doses from 760 to 841 r, using the sets of conditions A, B, C, D, E, and F of Table 1 in the preceding paper.[2] The survival times between irradiation and death were recorded, and the data obtained assembled in Figure 1. Every symbol represents an individual observation; its position indicates weight at the time of irradiation, and survival time. It was found that for mice up to 9.5 gm., the survival time is about three and one-third days, a plateau value established in the preceding paper.[2] For mice of greater weights, the survival times are directly proportional to the weight. In the transitional zone, between the two segments of the curve, there is the same appearance of uncertainty which was observed in the transitional zones of the curve showing the effect of various doses on mice of a given weight.

Similar results were obtained with higher and lower doses. Figure 2 shows the survival times observed in 40 mice after administration of 1,110 and 1,120 r (settings



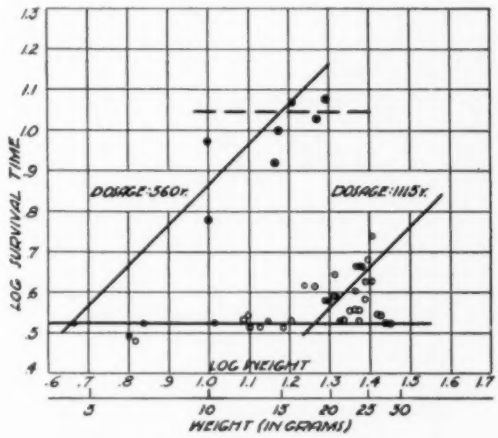


FIG. 1 and 2. Survival time as a function of weight, for constant doses. Circles represent individual observations, heavy lines the estimated trends. Fig. 1, doses of 800 r, 5 per cent; Fig. 2, doses of 560 and of 1,115 r. The scales in these (and all the other graphs except Fig. 3 and 4) are logarithmic for greater ease in presentation. The formulae and figures in the text are numerical.

* From the Department of Radiology, Carle Hospital Clinic, Urbana, Illinois.

D and F), and the survival times in 7 mice killed out of 10 irradiated with doses of 558 and 560 r (settings A and F). With the low doses, the entire weight range studied corresponds to the sloping segment of the curve, whereas with the high doses, the plateau extends up to near the upper limit of the weight range.

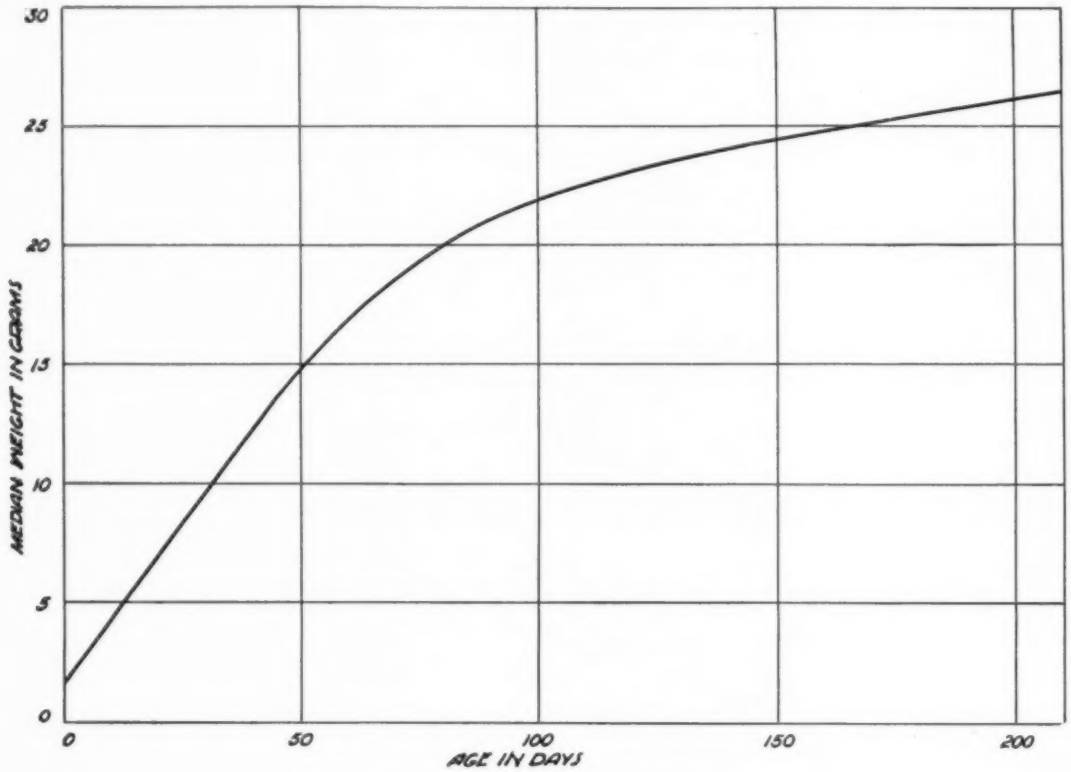


FIG. 3. Age and median weight (C57-Black mice).

In mathematical terms, the relation between survival time and weight, at a given dosage, can be expressed as follows:

$$T = 3\tfrac{1}{3} \text{ days} \qquad (W \leqq A) \tag{2.1}$$

$$T = k.W \qquad (W > A) \tag{2.2}$$

where T is the survival time between irradiation and death, W the weight at the time of irradiation, and k and A are functions of the dosage.

For the zones of the subacute and hyperacute reactions we have not enough observations to formulate the results quantitatively. It can be stated, however, that in these two zones the situation is at least qualitatively the same as in the zone of the acute reaction. Lighter mice die earlier than heavier ones in both zones.

To summarize the influence of weight on survival time: In regions where the response changes with varying dose, mice will survive longer in proportion to their weight after administration of equal doses; or, to obtain equal survival times, the doses have to be higher for the heavier mouse. On a plateau level, large and small mice die at the same time provided the dose is within the plateau range for all of the mice tested.*

WEIGHT AND AGE IN THEIR RELATION TO EACH OTHER AND TO SENSITIVITY

The mice used in our experiments were up to seven months old, the median weight increasing with age as shown in Figure 3.†

* Ellinger[1] has found no relation between survival time and weight in goldfish, but he does not state whether or not the dosage used was within the plateau range.

† The median weight divides the mice of any given age class into a heavy and a light group of equal size. The curve given is

From the two known relations, that between age and weight and that between weight and survival time, one can calculate the relation between age and survival time. This was done for a dosage of 800 r. Figure 4 shows the hypothetical curve of the age-survival time relation, together with symbols representing actual observations. Considering first only mice twenty-five or more days old, we see that the actual observations are near the expected values. The amount of scattering is about the same as that observed for the weight-survival time relation. Thus, age or weight could be used equally reasonably to predict the reaction of a given mouse to a given dosage. We use weight because it leads to a much simpler mathematical expression than age would.

For very young mice, those under twenty-five days old, the statement that sensitivity decreases with increasing weight does not hold true. Infant mice survive a given dose considerably longer than adult mice (dashed line in Fig. 4). A detailed discussion of these anomalous responses will be given in a later paper.

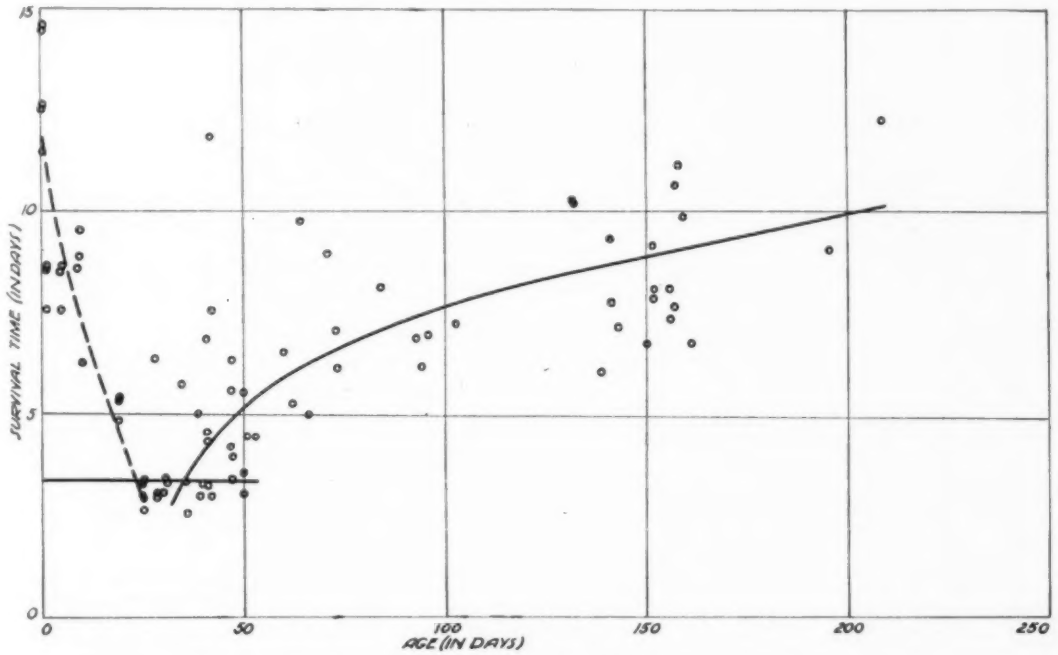


FIG. 4. Survival time and age. Symbols represents individual observations; full lines the trend as predicted from the two relations, between survival time and weight, and between weight and age; the dashed line the trend found in infant mice.

THE MEDIAN SURVIVAL TIME AS A FUNCTION OF DOSAGE AND WEIGHT

Combining the relations between dosage and survival time at a constant weight,

1.2 $\ldots T.D^2 = 4.64 \times 10^6 \quad \ldots (D \leqq 1175$ r for mice of 20 gm.)

1.3 $\ldots T = 3\frac{1}{3}$ days $\quad \ldots (D > 1175$ r)

and between weight and survival time at a constant dosage,

2.1 $\ldots T = 3\frac{1}{3}$ days $\quad \ldots (W \leqq A)$

2.2 $\ldots T = k.W \quad \ldots (W > A)$

we obtain the following formulae for the relation between survival time, dosage, and weight:

$$T.D^2/W = 2.3 \times 10^5 \quad (D^2/W \leqq 6.9 \times 10^4 \text{ r}^2\text{gm}^{-1})$$
$$T = 3\tfrac{1}{3} \text{ days} \quad (D^2/W > 6.9 \times 10^4 \text{ r}^2\text{gm}^{-1})$$

and, assuming that the survival time-weight relation holds true for all four seg-

not identical with the growth curve of any given mouse. Individual growth curves show an inflexion at about 15 gm. which is much sharper than that of the "median weight" curve. Also, they often show irregular oscillations around the region of inflexion.

ments of the dose-response relation, we get the set of formulae:

2.3 . . . $T = 11\frac{1}{2}$ days
. . . $(D^2/W \leqq 2.1 \times 10^4 r^2\ gm^{-1})$

2.4 . . . $T.D^2/W = 2.3 \times 10^5$
. . . $(2.1 \times 10^4 < D^2/W \leqq 6.9 \times 10^4\ r^2\ gm^{-1})$

2.5 . . . $T = 3\frac{1}{2}$ days
. . . $(6.9 \times 10^4 < D^2/W \leqq 6.7 \times 10^6\ r^2\ gm^{-1})$

2.6 . . . $(\log T - 1.05) \times (\log D^2/W - 7.8) = 0.25$
. . . $(6.7 \times 10^6 < D^2/W)$

6. The observations are scattered around the mean, 2.3×10^5, with a standard deviation of 19 per cent. The distribution is skew but this might not hold true with a larger number of observations. A small part of the scatter can be traced to the experimental factors, errors in the determinations of dose and survival time, and incidental fluctuations of the weight. However, the

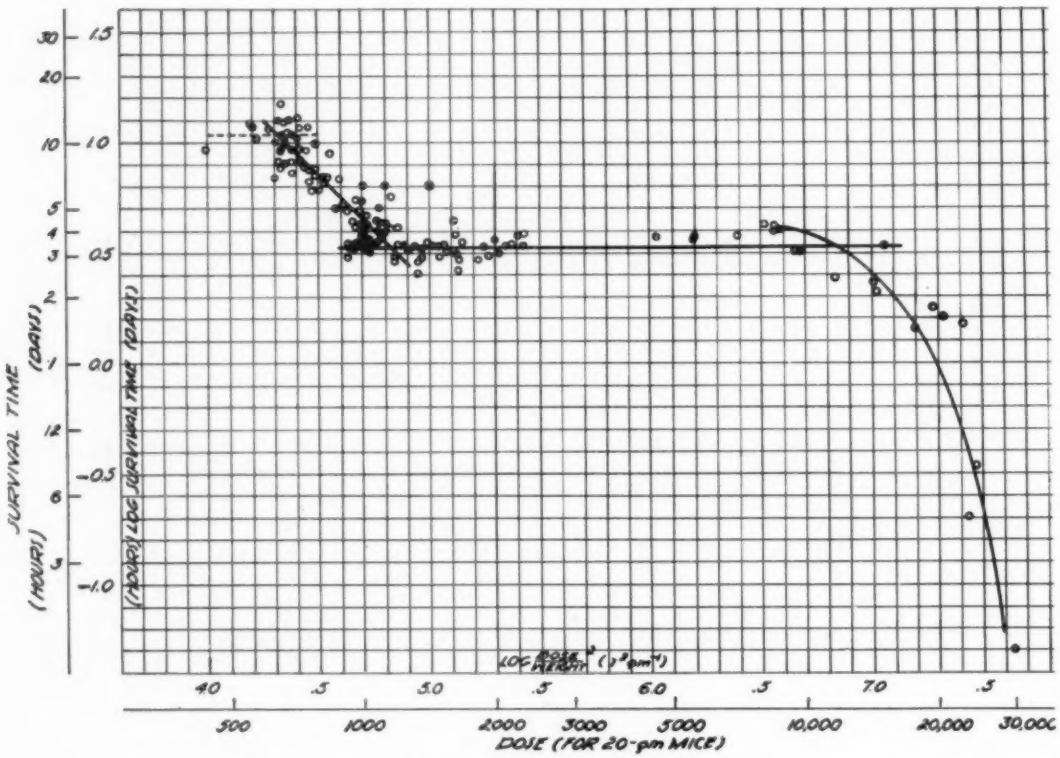


FIG. 5. Survival time as a function of the quotient "squared dose over weight."

These formulae are represented by heavy lines in Figure 5. The symbols indicate 202 individual observations in C57-Black mice. The agreement between observed values and the curve is good.

A quantitative study of agreement between observed and expected values was performed for the second, sloping segment of the curve. In this zone, the dose-response relation is expressed by the formula, $T.D^2/W$ equals a constant. Excluding the transitional zones, we find 33 mice in this region. The actual values, $T.D^2/W$, observed in this group, are entered in Figure 6. The observations are scattered around the mean, 2.3×10^5, with a standard deviation of 19 per cent. The distribution is skew but this might not hold true with a larger number of observations. A small part of the scatter can be traced to the experimental factors, errors in the determinations of dose and survival time, and incidental fluctuations of the weight. However, the largest part of the deviations, about 17 per cent, is unaccounted for.

DISCUSSION

The investigation of survival times in relation to weight and dosage has demonstrated two facts: adult mice of various weights show essentially the same reactions, with identical plateau values; and heavier mice are less sensitive than lighter ones. For given doses, the quotient of survival times equals the quotient of the respective weights, provided the survival times are off the plateaus.

As far as we know, no such definite relation between body weight and roentgen-ray effects has been established before. A weight factor like the one we discussed appears very commonly in the study of drug actions. But it must be remembered that the quotient dose (of a drug) per body weight, in pharmacology, is analogous to the plain dose in total body irradiation. Both indicate the average concentration of an agent in the body tissues.* Thus, the explanation of the protective influence of weight is not obvious.

A possible relation which we have to discuss is the one between speed of growth and sensitivity. It is generally true that the faster a tissue grows, the more sensitive it is to radiations. It is also true that the heavier a mouse is, the slower its growth, and the lower its sensitivity to roentgen rays. Yet, it is highly improbable that a direct connection between sensitivity and speed of growth exists. The growth curves show sharp inflexions around 20 gm., and these inflexions turn up whether we consider the absolute or the relative speed of growth. But they are not reflected in any comparably sudden change of sensitivity. Besides, there is the anomalous behavior of infant mice. They respond to irradiation less than adult mice, yet their growth is very vigorous. Thus, there cannot be any simple connection between growth and sensitivity.

SUMMARY

1. The survival time, after administration of constant doses, is proportional to the weight, provided the survival time is between eleven and one-fourth and three and one-third days.

2. The two plateaus, at eleven and one-fourth and three and one-third days, occur in adult mice of all weight classes.

3. The three relations, between age and sensitivity, between age and weight, and between weight and sensitivity, are concordant in adult mice.

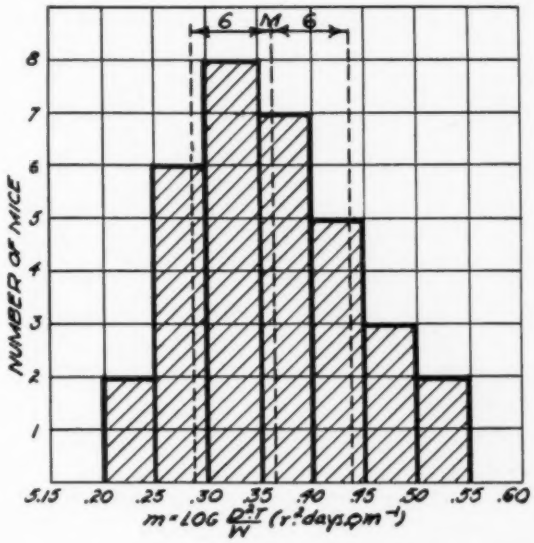


Fig. 6. Distribution of the value "squared dose by survival time over weight" in thirty-three C57-Black mice.

4. Infant mice survive longer than adult mice after application of the same dose.

5. Simple mathematical formulae for the relations between dosage, weight, and survival time are given.

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* The roentgenological term which compares to the plain "dose" in pharmacology is the volume dose, i.e., the integral of the dose distribution function over the irradiated volume. In total body irradiation, with homogeneous dosage distribution, the volume dose equals the product of dose by body weight.

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PNEUMOROENTGENOGRAPHY WITH OXYGEN IN THE DIAGNOSIS OF INTERNAL DERANGEMENTS OF THE KNEE JOINT*†

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THE use of contrast roentgenography in the diagnosis of internal derangement of the knee joint is by no means an original subject. Its use as an adjunct to clinical examination has been described previously.[1,2,4,5]

Because of the frequency with which we were encountering disability of the knee joint, where the physical examination presented little evidence of a pathological condition and the routine roentgenograms were not helpful, we attempted to better visualize the intracapsular soft tissues of the knee by the introduction of oxygen into the synovial cavity.[4]

At first both knees were examined simultaneously. It seemed best to carry out the bilateral procedure on the first few cases until we became well acquainted with the normal appearances and variations of the knee joint as visualized by pneumoroentgenography.

We do not believe that the procedure should be used without serious consideration or that every case that comes to the clinic with knee complaints should be subjected to it. However, in those cases where clinical evaluation is not conclusive, the method is thought to have definite diagnostic value.

In our series, 25 cases were examined, of which 18 knees were thought to show some abnormality. Of these 18, three had had the meniscus removed previously, and the resulting pneumoroentgenograms were thought to clearly demonstrate the complete absence of the meniscus in 2 cases. One was thought to show a residual portion of the posterior segment of a previously removed cartilage. This was later proved by operation.

Of the remaining 14 where abnormality was demonstrated 10 came to operation. In 9 cases the operative findings agreed completely with the roentgen diagnosis.

Failure to make the correct diagnosis in the tenth case we feel was due to insufficient removal of synovial fluid. Thus "filling" with oxygen was incomplete and poor visualization of the internal structures of the knee resulted. We were hesitant about giving an opinion in this case, and it demonstrated to us the need for a good "filling" before this procedure can be of diagnostic value.

In an eleventh operative case no abnormality was demonstrated on the pneumoroentgenograms. However, the clinical picture so strongly indicated a pathological condition of the medial cartilage that the suspected meniscus was exposed by operation. A loose segment was found to be attached to the thin inner edge of the medial third of the cartilage. On review of the pneumoroentgenograms we did not feel we could honestly say the abnormality as found at operation was demonstrable on the pneumoroentgenograms.

The remaining 4 patients with abnormal findings in the pneumoroentgenograms either refused operation or the clinical aspect of the case did not warrant surgery.

ANATOMICAL CONSIDERATIONS

In studying the knee joint from the standpoint of pneumoroentgenography, the following anatomical considerations are considered worthy of mention.

* From the Departments of Surgery and Radiology, Royal Canadian Navy Hospital, Sydney, N. S.
† Prints of roentgenograms and photographs by the Royal Canadian Navy Photographic Section.

The articular surfaces of the condyles of the tibia are smooth areas on the upper aspects of these structures and are separated by the intercondylar eminence. In front and behind the latter are roughened depressed triangular areas. The mesial articular surface is oval and depressed in the center. The lateral is more circular in outline and the central portion tends to be *slightly elevated* rather than depressed like the medial one. This results in the lateral cartilage being visualized more readily than the medial one. The lateral surface is prolonged backward and downward over the posterior aspect where it comes in contact with the popliteus tendon.

The articular capsule is a complicated structure. In front, the ligamentous formation is made up by an expansion of the quadriceps extensor tendon which ensheaths the patella. Below, the central fibers form the thick patellar tendon which is attached to the tibial tuberosity. The more mesial and lateral fibers are attached to the anterior aspect of the tibial condyles.

The back of the joint is covered by a ligamentous network of intersecting bands which form a posterior ligament. There is an opening laterally for the escape of the popliteus tendon. From its attachment, to the lateral aspect of the external femoral condyle, this tendon runs backward, downward and medially to emerge from the joint posteriorly.

The medial collateral ligament or the tibial collateral ligament is a broad flat band. It is a true capsular ligament and its upper aspect is attached to the medial epicondyle of the femur with some fibers merging into the adductor magnus tendon. Distally the ligament is attached to the medial surface of the tibia. The deepest fibers of this structure have a shorter course and are attached firmly to the medial meniscus which is well demonstrated in the arthrogram.

The fibular collateral ligament, on the lateral aspect of the joint, is a cord-like structure that is *definitely separated from the capsular ligament.* It is attached above to the lateral epicondyle of the femur and below to the head of the fibula. The true capsular fibers have a definite space between them and the fibular collateral ligament. The outer fibers of the capsular ligament are shorter and weaker and bridge the space between the femoral and tibial condyles. The inner fibers are attached loosely to the periphery of the lateral meniscus except in its posterolateral aspect where the popliteus tendon separates these two structures.

The intra-articular ligaments are the anterior and posterior cruciate ligaments which are invested by the synovial membrane extending from the posterior aspect of the joint.

The anterior cruciate ligament arises from the mesial aspect of the roughened triangular surface between the anterior aspect of the two tibial condyles and run upward, backward and laterally to be inserted into the medial non-articular surface of the lateral femoral condyle. The posterior cruciate ligament arises from the lateral aspect of the posterior non-articular surface and runs upward, forward and medially to be inserted into the lateral non-articular surface of the medial condyle of the femur.

The two menisci or semilunar cartilages are interposed between the femoral and tibial condyles. Each is a wedge-shaped crescentic fibrocartilage. The thick outer borders are bound down to the peripheral margins of the articular surfaces of the tibial condyles by the short fibrous coronary ligaments. These borders are also fused to the deep aspects of the medial and lateral capsular ligaments. Thus, the medial meniscus is much more firmly attached to the corresponding collateral ligament than the lateral as previously described.

The synovial membrane is extensive and invests all surfaces. The joint is partially subdivided by these investments into upper and lower compartments by the menisci and into medial and lateral compartments by the patellar folds in front and the cruciate ligaments behind. This is of importance in the removal of fluid in preparation for the introduction of oxygen as these subdi-

visions tend to hold collections of fluid and thus prohibit good soft tissue visualization.

Three large recesses are usually found: the suprapatellar synovial pouch and one behind each femoral condyle. There is an extension of the synovial pouch of varying lengths along the popliteus tendon as it leaves the joint. This extension communicates occasionally with the synovial cavity of the upper tibiofibular articulation. Additional bursae or recesses are described in textbooks of anatomy but are not usually seen in the pneumoroentgenograms.

SURGICAL CONSIDERATIONS

Introduction of oxygen into the knee joint, while a minor surgical procedure, should be carried out in the operating room under aseptic technique.

The anterolateral approach to the joint has been used in all our cases. A point is taken on a level with the superior margin and about 1 cm. lateral to the lateral border of the patella. Under local novocain infiltration, a No. 20 gauge spinal needle is inserted into the skin at this point and directed downward and medially toward the center of the patella. On entering the joint, a diminution in resistance is noted much as in a spinal puncture. A spinal needle is used, because, due to its length, it is more easily directed and the stylet insures less damage to tissue.

When the joint has been entered, a syringe is applied and an attempt at aspiration is made. This should always be done, as unsatisfactory filling with oxygen will occur if there is increased fluid present.

Following attempted aspiration a 3-way stopcock is attached to the spinal needle. A sterile length of rubber tubing is inserted into one of the apertures of the stopcock by means of a glass or metal connecting piece, and the other end is handed to an orderly who attaches it to the outlet of an oxygen tank.

A dry 50 cc. glass syringe is now inserted into the other aperture of the stopcock. With the valve placed so that the oxygen tank communicates with the syringe, an assistant slowly releases the oxygen until the syringe plunger is pushed back to the 50 cc. or desired mark. The valve is then turned so that the syringe communicates with the spinal needle and joint cavity. It is necessary that the syringe plunger be dry so that any change in the resistance necessary to inject oxygen into the joint may be easily detected. It is for this reason that a separate syringe is used for attempting aspiration.

As the first part of the oxygen is being injected it has been found useful to note the medial parapatellar sulcus for bulging. This bulging, together with the ease with which the gas is injected, will indicate that the oxygen is entering the joint satisfactorily. Also, tapping the patella to elicit resonance is useful, and this sign is present after the injection of a very few cubic centimeters of oxygen.

It has been found that about 100 to 140 cc. is the optimum amount of oxygen necessary for good filling. However, as we progressed in our series, good filling was best obtained where our experience allowed us to assess the general bulging about the joint and the quality of resonance elicited on tapping the patella, rather than by injecting a measured quantity of oxygen.

Collodion is applied to the needle puncture site, and the patient taken to the roentgen department on a stretcher, arrangements having been made previously so that as short a time as possible elapses between injection of the oxygen and the taking of the pneumoroentgenograms. This time factor was not at first thought to be important, but we are satisfied that optimum roentgenological visualization is best obtained as soon as possible after the introduction of the gas.

Following roentgen examination the patients are returned to the ward with crepe bandages firmly applied. They are allowed up and about on the following day with no restriction of activities. Resonance on tapping the patella is present for about three to four days.

One patient developed an effusion four

days following the introduction of oxygen. Forty cubic centimeters of turbid fluid was aspirated. Large numbers of polymorphonuclear cells were present, but no organisms were found on smear or culture. Swelling regressed following aspiration and did not recur. No other complications following pneumoroentgenography have been encountered.

In 2 of our cases poor filling with gas was present in the symptomatic knee. Pneumoroentgenography was repeated, and in both cases abnormal amounts of fluid were present. Aspiration and reinjection of gas produced excellent pneumoroentgenograms. Thus, whether the presence of increased fluid content is suspected or not, aspiration should be attempted in every case prior to injecting oxygen.

PNEUMOROENTGENOGRAPHIC TECHNIQUE

A tight elastic bandage is applied to compress the suprapatellar recess and thus force as much gas as possible down into the joint space proper. The bandage should be applied starting well up above the knee gradually working down to include at least the upper half of the patella.

The exact position of the knee joint is located under the roentgenoscope and is well marked on both sides with skin pencil. It is considered better to apply the bandage before roentgenoscopy because of the relative change in position of skin and bone structures caused by the tight bandage. At this point it should be stated that if the knee joint does not appear to be well filled with gas under the roentgenoscope there is little use in going further with the examination. Careful observation at this time will save the roentgenologist considerable time.

The knee is next placed in an anteroposterior position over a specially built curved cassette holder (Fig. 1) which allows approximately 30° flexion of the joint. This dorsal position with the 30° flexion of the knee produces a spread of the joint space and thus better visualization of the internal soft tissue structures. It is believed that the curved film distorts the image in such a manner that the knee joint proper is widened to an appreciable extent. It is also considered that the use of the dorsal position and the curved cassette results in closer apposition of the joint to the film which allows finer detail on the pneumoroentgenogram. In this position it is easy to take the external and internal rotation oblique views with a maximum of comfort and a minimum of movement.

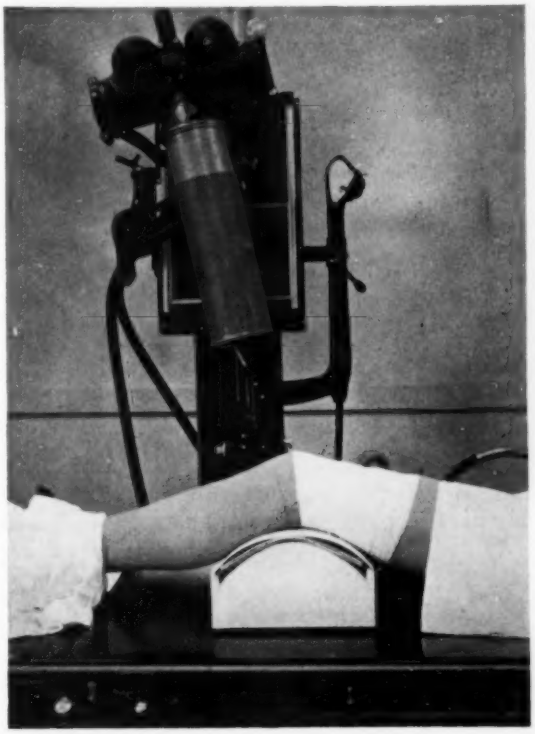

Fig. 1. The curved cassette holder with the cardboard film folder in place under the knee joint.

The choice of the actual projections used rests with the roentgenologist concerned. Our routine projections were all stereoscopic sets in the dorsal, 45° external rotation, 45° internal rotation and true lateral views.

It was only after considerable experiment in different positions both with and without the curved cassette holder and in various projections that it was decided to use the above technique. The positioning as described by Cullen and Chance[2] was tried on a number of our cases. We found it gave

good visualization of one meniscus; however, it left much to be desired in demonstrating the other meniscus of the joint in question. Thus, since there is frequently some doubt as to which meniscus is involved the procedure is not used routinely.

All exposures were made with an extension cone of 10 cm. diameter at 30 inch focal skin distance, with 60 to 63 kv. (peak) at 100 to 125 ma-sec. on extra-speed film in cardboard holders. Where non-screen high speed film was used, which gave us better

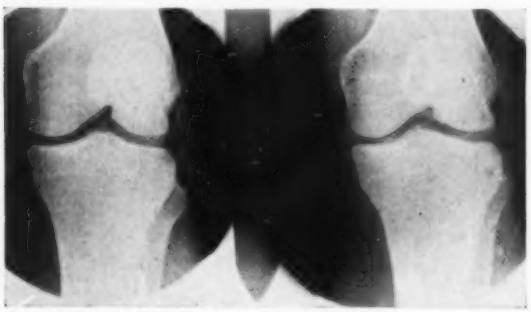

FIG. 2. The pneumoroentgenogram of the right knee demonstrates the angulated uninterrupted air column extending along the tibial collateral ligament and the increased density between the lateral halves of the articular surfaces of the medial condyles.

soft tissue detail, 20 to 30 ma-sec. proved to be sufficient with the other factors unchanged. The central ray is projected through the previously marked joint space which requires a 10 to 15 tilt of the tube cephalad.

INTERPRETATION OF THE NORMAL PNEUMOROENTGENOGRAM OF THE KNEE JOINT

In the pneumoroentgenogram the cartilaginous covering of the bony articular surfaces is usually well demarcated and it is smooth and evenly distributed over all areas.

The numerous synovial folds and prolongations are best visualized in the lateral position. The most readily demonstrated are those behind the infrapatellar fat pad and in the posterior aspect of the joint. The suprapatellar recess contains a surprising amount of gas considering the pressure with which the bandages are applied as demonstrated in the left knee of Figure 4. Good filling of the pouch behind each femoral condyle is usually procured.

In the anteroposterior view the medial cartilage is not as well outlined in its entirety as the lateral, as illustrated in the right knee of Figure 4. This is due to its firmer attachments to the tibial collateral ligament which is well demonstrated. The short coronary ligaments bind this cartilage down tight to the tibial articular surface. Occasionally one sees a small air pocket under the mesial periphery of the cartilage as visualized in the left knee of Figure 7. The superior surface of the cartilage is really the only one well outlined and it can usually be easily differentiated from the articular surface of the medial femoral condyle again seen in the left knee of Figure 7. Normally the anterior and posterior horns of this cartilage are hard to demonstrate.

The lateral semilunar cartilage is usually better outlined than the medial. Its attachment to the lateral aspect of the capsule is visualized but is not as broad or firm as the corresponding one of the medial cartilage. An air column is usually seen to follow the popliteus tendon up behind these loose lateral attachments. This column demonstrates well the lack of fibers attaching the lateral meniscus to the lateral ligament of the capsule because of the interposition of the tendon. This is best seen in the oblique views of the left knee of Figure 3.

This cartilage frequently appears to ride higher in the joint space having only its weak lateral and its mesial anterior and posterior horn attachments. Thus both the superior and inferior borders of the meniscus are well visualized.

The cruciate ligaments can usually be demonstrated in respective positions. The anterior running upwards and laterally, the posterior upwards and medially. The latter is usually better visualized because of its more "end on" projection.

INTERPRETATION OF THE ABNORMAL PNEUMOROENTGENOGRAM OF THE KNEE JOINT

1. *Avulsion of the Internal Cartilage from*

its Medial Capsular Attachments (Fig. 2). In comparing the bilateral pneumoroentgenograms of this case, those of the right knee presented an irregular but nevertheless an uninterrupted air column extending along the medial aspect of the knee joint. An increase in density of soft tissue between the lateral halves of the medial condyles is noted. Loss of soft tissue shadow and narrowing characterizes the medial half of the joint space.

The roentgen diagnosis was avulsion of the normal medial capsular attachments of the right medial meniscus with displacement of the cartilage into the central aspect of the joint.

At operation the medial cartilage was completely separated from the collateral ligament shifting laterally and acting as a loose body impinging between the medial condylar articular surfaces. The periphery of the meniscus was moth eaten and narrowed.

2. *Avulsion of the Anterior Horn of the Medial Cartilage from the Tibial Attachments* (Fig. 3). The pneumoroentgenograms of this case present in the internal oblique view of the left knee a well defined cartilage shadow. As one follows it in towards the intercondylar eminence it is noted that instead of following closely along the superior aspect of the tibia it swings up to be lost in the shadow of the condyle of the femur.

Fig. 3. In the left knee note the upward displacement of the shadow of the medial cartilage as it extends medially.

This was interpreted as being a mesial cartilage that had lost its anterior tibial attachments.

At operation the anterior horn of the mesial cartilage was found to be completely avulsed from its normal tibial attachments. Instead it was riding free in the joint cavity.

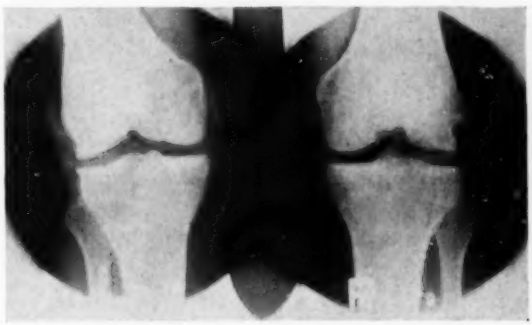

Fig. 4. The uninterrupted column of air inside the lateral collateral ligament and the shadow of the semidetached lateral cartilage interposed in the intercondylar space medially are well shown in the left knee.

3. *Avulsion of the External Cartilage from the Lateral Capsular Ligament and Displacement into the Joint* (Fig. 4). In the dorsal pneumoroentgenograms of this case an uninterrupted column of air is seen to extend up along the lateral ligament of the left knee joint. No normal lateral meniscus shadow is observed but rather the joint space is definitely narrowed with eburnation of the contiguous articular surfaces. A dense elongated soft tissue body is seen to be floating below the intercondylar region of the femur.

In the external oblique pneumoroentgenograms (Fig. 5) two well circumscribed "punched out" like areas are noted in the anteroinferior aspect of the left lateral condyle of the femur. These were suspected in the routine roentgenograms but were not felt to be definite enough to give an opinion.

Our diagnosis from these films was that the left lateral cartilage had lost all its normal attachments to the lateral ligament of the joint capsule and had shifted medially into the middle of the joint space with only its anterior and posterior horn attachments intact. Osteochondritis dissecans involving

FIG. 5. The left knee exhibits well demarcated areas of increased radiolucency in the lateral condyle of the left femur just posterior to the tip of the patella.

the lateral femoral condyle was the interpretation of Figure 5.

At operation the left lateral cartilage was as described above and the areas of osteochondritis were confirmed. The medial meniscus was normal.

It is worth noting that this case clinically was considered to have medial meniscus abnormality and it was with considerable reservation that the incision was made to expose the lateral aspect of the joint.

4. *Loose Bodies, Pedunculated or Otherwise, in the Knee Joint.* In this case no definite abnormality was at first seen in the pneumoroentgenograms. However, as the patient had such definite clinical symptoms the knee joint was opened on the medial side. A pedunculated loose portion of the anterior segment of the medial cartilage was found.

The appearance of the internal oblique pneumoroentgenograms (Fig. 6) would, we feel on review, support such a diagnosis. In these films a triangular shaped area of increased density is noted above the inner portion of the medial cartilage. This, it is believed, is the shadow of the loose portion of the cartilage found at operation.

Since the above case we have had 2 cases which at operation exhibited a similar condition. One case was diagnosed by pneumoroentgenography, the other was not.

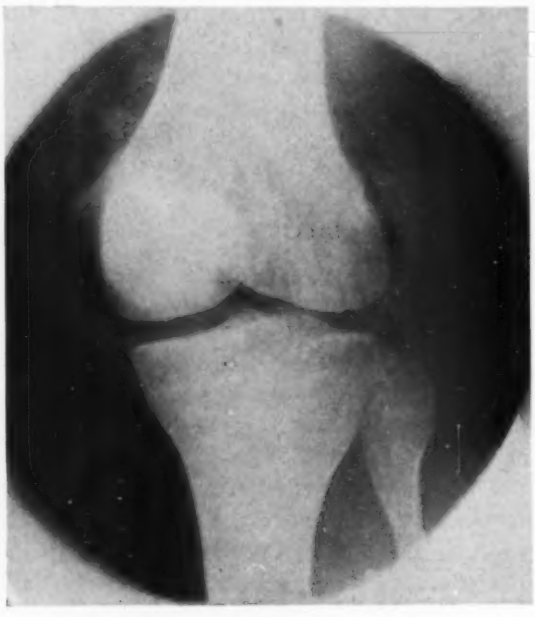

FIG. 6. Note the triangular shaped shadow above the inner aspect of the internal semilunar cartilage.

FIG. 7. In the right knee the absence of cartilage shadow and the uninterrupted air column are characteristic of the joint appearance following removal of the cartilage.

5. *Surgically Removed Cartilage.* Cases that have had a cartilage removed resemble very much the avulsion type as described in Figures 2 and 3.

In the true dorsal and the dorsal oblique pneumoroentgenograms there is visualized an interrupted column of air inside the lateral capsular ligament. There is lack of soft tissue shadow between the articular surfaces of the condyles. All these points are demonstrated in the accompanying right pneumoroentgenogram (Fig. 7).

SUMMARY

In the cases presented the classical symp-

toms of internal derangement of the knee were not exhibited. In some instances the acute symptoms had subsided and the physical examination presented very little evidence of a pathological condition. Thus we were dependent to a great extent on the history of previous episodes. In an attempt to avoid long periods of observation in the hospital, these patients were subjected to oxygen pneumoroentgenography. It is believed that this procedure has facilitated an early decision relative to surgery in these cases.

We have found the following points to be of diagnostic value in the interpretation of pneumoroentgenograms of the knee joint:

1. Roughening and narrowing of cartilage surfaces, either articular surface coverings or the semilunar cartilages as visualized in the left knee of Figures 4 and 5.

2. Uninterrupted gas columns along the inner aspect of the collateral ligaments of the joint where capsular structure should be firmly attached to the periphery of the menisci. This is demonstrated in Figures 2, 4 and 7. The normal gas column presented on the posterolateral aspect of the knee joint by the popliteus tendon should be kept in mind.

3. Increase in the soft tissue (increased density) in the intercondylar or non-articular region of the joint with a corresponding lack of density in the lateral or medial region, as demonstrated in Figures 2 and 4.

4. Separation of the meniscus shadow from the contiguous bone structures illustrated in Figure 3.

5. Loose or semi-loose bodies calcified or otherwise shown in Figure 4.

6. Joint space narrowing as visualized in Figure 4.

7. Exostosis and eburnation of the articular surfaces as seen in Figures 4 and 5.

The last three findings can be demonstrated on routine reontgenograms of the knee. In each of our cases the ordinary roentgenograms were taken and although such conditions were suspected they were by no means as convincingly demonstrated as following the introduction of oxygen. This is more applicable to cases with early pathological changes of these types.

It has been of interest to us to demonstrate that the amount of cartilage left along the capsular attachment in the bucket-handle fracture has been much less than we would anticipate from the appearance of the pneumoroentgenogram.

The lack of mention of any cruciate abnormality will of course be noted. None of our cases thus far encountered were thought to demonstrate definite cruciate abnormality on the pneumoroentgenograms nor were any such lesions found at operation. Thus, we are unable to give any information at this time with reference to cruciate ligament injury.

CONCLUSIONS

1. Oxygen pneumoroentgenography is a useful adjunct in the diagnosis of obscure internal derangements of the knee joint.

2. It should not be used routinely but only in those cases which present a difficult diagnostic problem.

3. Calcified and more especially non-calcified loose or semi-loose bodies (joint mice) are clearly demonstrated.

4. The procedure when performed under aseptic surgical conditions carries little risk of complications.

5. The use of the curved cassette holder and multiple stereo projections has, in our opinion, increased the accuracy and usefulness of this procedure.

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MINIATURE CHEST FLUOROGRAPHY WITH CONTROL STUDY*

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MANY reports have appeared in the literature in recent years to indicate the value of miniature chest fluorography for the detection of pulmonary tuberculosis. Relatively few studies have been made to confirm the accuracy of this method by simultaneous roentgenography with the conventional 14 x 17 inch film. Potter, Douglas and Birkelo[9] examined 1,610 clinic attenders in this manner using single 4 x 5 inch films as the miniature record. These patients either had symptoms of tuberculosis, had been exposed to it, or had had a positive skin test for tuberculosis. There was only a 2.6 per cent error in detecting 271 cases with active tuberculosis as found on the full size film. Bridge[1] found 259 cases of significant tuberculosis out of 1,000 consecutive cases examined by single 4 x 5 and 14 x 17 inch films in a tuberculosis dispensary. Two, or 0.77 per cent, of these cases were missed on the miniature films and of the 130 minimal lesions, 2, or 1.5 per cent, were in error on the smaller films. Plunkett, Weber and Katz[7] examined 1,000 patients in a mental hospital utilizing 35 mm., 4 x 5 and 14 x 17 inch films on each subject. On the 35 mm. films 91.8 per cent of clinically significant tuberculosis was detected and on the 4 x 5 inch films 98.3 per cent was found. In this study, the detection of minimal lesions was accurate in 82.6 per cent in the 35 mm. and 96.6 per cent in the 4 x 5 inch films.

The purpose of this communication is to submit further evidence of the accuracy of findings in 1,000 subjects consecutively examined by the 4 x 5 inch miniature method in comparison with the 14 x 17 inch film used in regular practice. It is generally agreed that the use of stereoscopic 14 x 17 inch roentgenograms is the most accurate method for the diagnosis of minimal pulmonary tuberculosis. Christie[2] and de Lorimier[3] are of the opinion that stereoscopic 4 x 5 inch fluoroscopic roentgenograms are of greater diagnostic accuracy than a single 14 x 17 inch roentgenogram because the shift of the roentgen tube will uncover small lesions hidden under the rib shadows. The present study indicates that even the single 14 x 17 inch roentgenogram is superior in diagnostic qualities to the stereoscopic 4 x 5 inch miniature.

A photoroentgen unit was installed in the Department of Roentgenology at the University Hospitals of Cleveland to reduce the cost entailed in examining the chests of employees who constitute an unselected, apparently healthy adult group. While it was realized that the 35 mm. unit has certain advantages over other types of miniature apparatus, such as in reduced cost, speed of operation and smaller filing space of films, the 4 x 5 inch type was nevertheless selected because it seemed to be more practicable for our purpose based on the experience of other workers (Christie, de Lorimier, Plunkett, Weber and Katz, Bridge, and Potter, Douglas and Birkelo). The cost of the smaller film is about one-sixth that of the conventional size without consideration of the saving in processing.

Miniature and large roentgenograms were simultaneously obtained on the first thousand asymptomatic subjects consecutively examined.

TECHNIQUE

Experimentation with this new method of examining chests demonstrated that certain technical factors are more exacting

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than in conventional roentgenography in order to obtain satisfactory results. Emphasis is placed on accurate measurements of the anteroposterior diameter of the chest for variations in kilovoltage and on precise centering of the patient's chest against the screen support. The only variable factor is peak kilovoltage which ranges between 61 and 74. The constant factors include a current level of 300 milliamperes, 42 inch focal-screen distance, $\frac{1}{5}$ second exposure time, fine mesh stationary grid (50 lines per inch) and single emulsion film. The apparatus employed is the photoroentgen unit manufactured by the General Electric X-Ray Corporation for stereoscopic 4 x 5 inch films (single film in 4 x 10 inch holder). The fluorescent screen is composed of large crystals of zinc sulphide which has seven times greater illumination than the ordinary fluoroscopic screen. The camera lens is rated at F 1.5. Our own experiments with single and double emulsion films with and without a grid corroborate the findings of Potter[8] and de Lorimier[3] in that the most satisfactory roentgenogram from the standpoints of contrast and detail is obtained with the single coated film in conjunction with a grid. Equivalent results are obtained with either the Eastman or DuPont brand of film. Examinations of chests with anteroposterior diameters greater than 25 cm. were rejected since our experience, as well as others (Pindell[6]), has shown results to be uniformly poor.

Film manufacturers have advocated a slight increase in developing time for improvement in contrast. We have found that a slight increase in kilovoltage over the measured normal with developing time the same as for the average roentgenogram produces a slightly "underdeveloped" appearing film of improved diagnostic qualities.

The roentgenographic apparatus used in conjunction with the photoroentgen unit consisted of a General Electric K x 8 500 milliampere transformer with impulse timer and rotating anode tube of 2 mm. focal spot.

A specially designed stereoscope (orthostereoscope) is used for viewing 4 x 5 inch stereoscopic photoroentgenograms, giving the viewer the effect of scanning a 14 x 17 inch roentgenogram at a 40 inch distance. The position of the lenses is fixed in relation to films with adjustment allowed for different interpupillary distances.

TABLE I

	Original Interpretation			
	14" x 17"	Errors 14" x 17"	4" x 5"	Errors 4" x 5"
Minimal pulmonary tuberculosis	23	1	20	4
	Classification of Lesions After Review			
Active minimal tuberculosis	17	0	16	1
Inactive minimal tuberculosis	7	0	7	0

STATISTICS

The interpretations of the two sizes of roentgenogram were equally divided between the authors and the results compared later. One of us made reports on the first 500 fluorograms while the other interpreted the large roentgenograms made on the same employees. The procedure was reversed between us for the second series of both types of roentgenograms. Recordings were made on form sheets according to Hodges.[4]

In the interpretation of the miniature roentgenograms, the lesions were not classified as active or inactive. Only after review of the two sets of roentgenograms was this

classification made (Table 1). Of the cases examined 602 were females and 398 were males. The average age for both sexes was twenty-nine years, the females being twenty-six and the males thirty-three. The oldest was seventy-two and the youngest fifteen years of age. There were 24 cases of pulmonary tuberculosis, all of minimal extent, in the 1,000 subjects examined. Of these 24 cases, 11 were females and 13 were males. This incidence is higher than is ordinarily found in the adult population at

TABLE II

	14" x 17"	4" x 5"
Small shadows incorrectly called questionable tuberculous lesions	4	6

large and may be accounted for by the large number of student nurses in this group.

One error was made in the interpretation of the 14 x 17 inch roentgenogram while 4 errors were accounted for in the group of miniatures. In the review study, the lesions were classified as active and inactive minimal lesions, there being 17 of the former and 7 of the latter group (Table 1). Only one error was found on a miniature after the roentgenograms had been carefully compared. This roentgenogram failed to demonstrate the lesion even though it was readily observed on the large roentgenogram. The reason was due to a slight difference in angulation.

In this study there were several small shadows called questionable tuberculous lesions which on review proved to be incorrectly interpreted (Table 11). Two of these shadows proved to be blood vessels seen on cross section. Four others were calcified tuberculous foci. One of these cases was incorrectly interpreted on both the 14 x 17 and 4 x 5 inch roentgenograms. Such shadows, even though considered a questionable lesion, should be checked by large roentgenograms until greater experience in this type of work is gained.

A considerable number of diseases of the chest other than pulmonary tuberculosis were also found in this study. They include diseases of the heart and great vessels, pleural scarring, anomalies, pneumonia, acquired bone lesions, mediastinal masses, scoliosis, sarcoidosis, fibrosis of the lung, bronchiectasis, spontaneous pneumothorax

TABLE III

Diseases of heart and great vessels	22	Scoliosis	5
Pleural scarring	18	Sarcoidosis	2
Anomalies	17	Fibrosis of lung	2
Pneumonia	10	Bronchiectasis	1
Acquired bone lesions	7	Spontaneous pneumothorax	1
Mediastinal mass	5	Lung tumor	1

and lung tumor. Table III gives the number of these lesions.

SUMMARY

1. Many studies have been made to indicate the value of miniature chest fluorography, but only a few comparison studies with 14 x 17 inch roentgenograms have been reported.

2. Further evidence is submitted as to the accuracy of stereoscopic 4 x 5 inch miniature fluorography by the examination of the chests of 1,000 symptomless adult hospital employees with conventional roentgenographic control.

3. Precision in technique is necessary in miniature fluorography if satisfactory results are to be obtained.

4. Twenty-four minimal pulmonary tuberculous lesions were detected in 1,000 examinations. Four errors were made in the first interpretation of the miniature films. Only one error was recorded on review of both sizes of films indicating the accuracy of the method.

5. Experience in the interpretation of miniature films is necessary for the highest degree of accuracy.

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MILIARY CARCINOSIS OF THE LUNGS SECONDARY TO PRIMARY CANCER OF THE GASTRO-INTESTINAL TRACT

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MILIARY carcinosis of the lungs from cancer of the gastrointestinal tract, biliary tract and pancreas is not common. There are certain pathologic and anatomic reasons for this. These will be discussed briefly and then the necessary variations to produce miliary carcinosis will be formulated.

Of course, miliary carcinosis to the lungs requires blood stream dissemination of tumor cells to the right heart. Venous return from the gastrointestinal tract and associated structures passes by the portal vein to the capillary bed of the liver which, at least theoretically, should filter out tumor cell emboli in most instances with subsequent formation of secondary liver lesions. Thus, by this route, the tumor cells would not reach the pulmonary circulation. Lymphatic spread or direct extension alone could not possibly account for miliary pulmonary distribution. Pulmonary spread by lymphatics through the diaphragm could occur but the appearance in this case would not be that of miliary carcinosis either roentgenographically or pathologically. Rather, it would resemble the lymphatic pulmonary extension seen in cancer of the breast. Metastatic spread of cancer of the gastrointestinal tract is predominantly lymphatic as in other malignant tumors of epithelial origin. Such a spread is first to the regional lymph nodes. From there extension to the thoracic duct may occur with any degree of extension up this trunk. This extension into the neck accounts for the occurrence of a Virchow's node in malignant tumors of the gastrointestinal tract. Tumor cell emboli may pass from the thoracic duct to the left subclavian vein, to the left innominate, to the superior vena and then to the right heart where a massive blood stream dissemination to the lungs may occur. By this mechanism outlined above we have our first method of pulmonary miliary carcinosis from the gastrointestinal tract.

A second method is perhaps more common. If an extension from a primary gastrointestinal malignant tumor invades the liver and then the hepatic veins, multiple tumor cell emboli may enter the venous circulation and pass directly to the right heart and then to the pulmonary fields. Such a condition may be set up by direct extension to the liver as in cancer of the gallbladder or by secondary blood stream metastases by the portal circulation to the liver. Actual invasion of the hepatic veins can usually be demonstrated pathologically in these cases which show spread to the lungs.

It must be noted at this time that either of the above mechanisms may result in isolated pulmonary metastases and it is only when a large shower of tumor cells passes into the circulation that we have the necessary condition set up for an actual miliary carcinosis. Also we may have all variations between an isolated metastasis and a miliary carcinosis. This paper deals only with cases which exhibited a definite miliary carcinosis.

Secondary pulmonary extension may in some cases somewhat obscure the primary picture. This extension may be lymphatic or even bronchiogenic as tumor cells invade the alveoli and smaller bronchi.

Achard, Bariéty, Desbuquois and Sternfeld[1] in 1931 published a case of miliary carcinosis from a cancer of the stomach in which they concluded that the metastases were entirely of lymphatic spread. Desbuquois[2] published a second similar

case in 1935 with similar conclusions. Such a type of spread is not generally thought of in miliary carcinosis to the lungs although secondary involvement of pulmonary lymphatics is not uncommon, as has been mentioned previously. It would seem that anatomically a true miliary carcinosis must depend on blood stream dissemination through the right heart, the same as in miliary tuberculosis.

CASE REPORTS

Case 1. Mrs. L. D., female, white, aged sixty-three, admitted to the hospital on December 8, 1935. For one year previous to admission the patient had had intermittent dull pain in the left costovertebral angle and interscapular areas. She had also had occasional low abdominal pain. During the year prior to admission she had lost 20 pounds in weight and had noted increasing fatigability and loss of appetite.

Physical Examination. Temperature, pulse and respirations were normal. The patient appeared somewhat emaciated and slightly icteric.

The examination of the chest was essentially negative. The left lobe of the liver was palpable and slightly tender.

Laboratory Findings. Urinalysis showed presence of bile; otherwise, negative. Red blood count 4,900,000; hemoglobin 100 per cent; white blood count 15,000, with 75 per cent polymorphonuclear cells with a moderate left shift. Icteric index 50 per cent; van den Bergh test 6.4 mg. per 100 cc. Stools were negative for occult blood, positive for bile.

Roentgen Findings. On December 8, 1939, the gastrointestinal tract was examined and except for diverticulosis in the sigmoid colon no pathological condition was noted. The gallbladder was studied with oral dye and no function was noted. Chest examination on December 13 showed evenly distributed soft infiltrates throughout both lung fields varying from pinhead size to pea size. The distribution was that of a hematogenous spread.

Course. The patient remained in the hospital until December 23, 1939, at which time she was discharged, condition the same as on admission. The patient remained at home until March 8, 1940, at which time she was re-admitted to the hospital. During her stay at home her jaundice had become increasingly intense and she had had continuous pain in the left costovertebral angle. She had also noted increasing weakness. During the week previous to admission, nausea and vomiting had become prominent symptoms. Physical examination at this time showed marked increase in her degree of jaundice. Chest showed some dullness in the right base and numerous fine râles throughout the right chest. The abdomen was distended and physical findings of free fluid in the abdomen were demonstrable. The patient was markedly tender in the left flank and in the left costovertebral angle. She showed pitting edema of both feet and ankles.

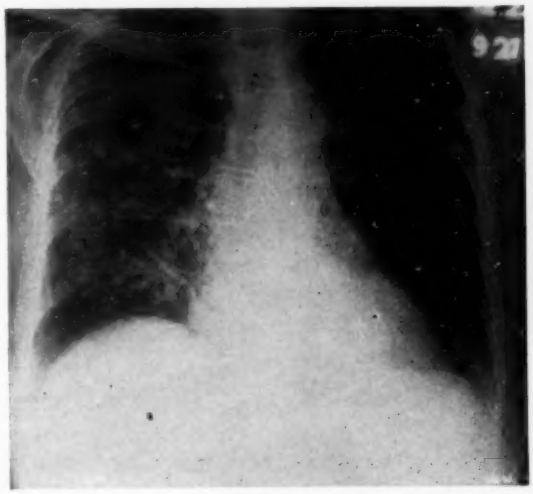

Fig. 1. Case 1. Roentgenogram of the chest.

Laboratory Findings at Second Examination. Urinalysis showed two plus albumin; positive for bile. Red blood count 3,000,000; hemoglobin 79 per cent; white blood count 34,000, with 93 per cent polymorphonuclear cells with a rather marked left shift. Icteric index 100 per cent plus; van den Bergh test 11.2 mg. per 100 cc. Stools showed four plus occult blood on all occasions.

The patient's course in the hospital was progressively retrogressive and she died on March 16, 1940.

Pertinent Autopsy Findings: Prosector—Dr. Kenneth Olsen. Primary cancer of the gallbladder with direct extension to the liver and diffuse metastases throughout the liver. Diffuse interstitial fibrosis of the pancreas. Diffuse evenly distributed pea-sized metastases were noted throughout all lobes of the lungs.

Pathological Diagnosis. Primary cancer of the gallbladder with direct extension to the liver

and with diffuse metastases to the liver and lungs.

Case II. D. R., female, white, unmarried, aged thirty-nine, admitted to the hospital on September 11, 1941. The patient had been previously admitted in December, 1935, with an acute nonspecific ulcerative colitis. She had a second admission in June, 1939, at which time a pseudomucinous cystoma of the right ovary was removed. One month prior to this admission the patient developed periodic attacks of generalized cramp-like abdominal pain which gradually increased in severity. Associated with this was increasing anorexia and constipation. During this month the patient lost 15 pounds in weight. For the four days before admission the patient had had repeated emesis.

Physical Examination. Temperature 99° F.; pulse 96; respirations 20. The patient did not appear acutely ill nor did she show evidence of marked weight loss. The abdomen revealed a well healed midline scar. There was moderate generalized abdominal tenderness. No physical findings were noted in the chest.

Laboratory Findings. Urinalysis showed a trace of albumin on several occasions. Red blood count 5,570,000; hemoglobin 91 per cent; white blood count 10,750; differential count showed a slight left shift. Glucose, urea, albumin, globulin, phosphorus and calcium normal. Icteric index and van den Bergh normal. Phosphatase normal. Sedimentation rate 23 mm. corrected. Gastric analysis showed free HCl present; no acid-fast bacilli after concentration. Stools were negative for occult blood.

Roentgen Studies. Flat roentgenogram of the abdomen did not reveal any abnormalities. Gastrointestinal tract was studied completely but there were no abnormal findings. Genitourinary tract was studied by retrograde pyelography which appeared normal. There was practically no visualization of the gallbladder by oral cholecystography. No stone shadows were discernible. The most remarkable findings were in the chest which on September 16, 1941, showed evenly distributed small mottled densities throughout both lung fields. They varied from pin-head size to pea size. Some areas tended toward confluency. The appearance was that of a blood stream spread of an infiltrative process to the pulmonary tissue. Inpression: Miliary carcinosis.

A roentgenogram of the chest on October 6, 1941, was similar to the previous examination except for progress in size of lesions and more confluency. Chest roentgenogram on November 28, 1941, showed further progress of chest lesions.

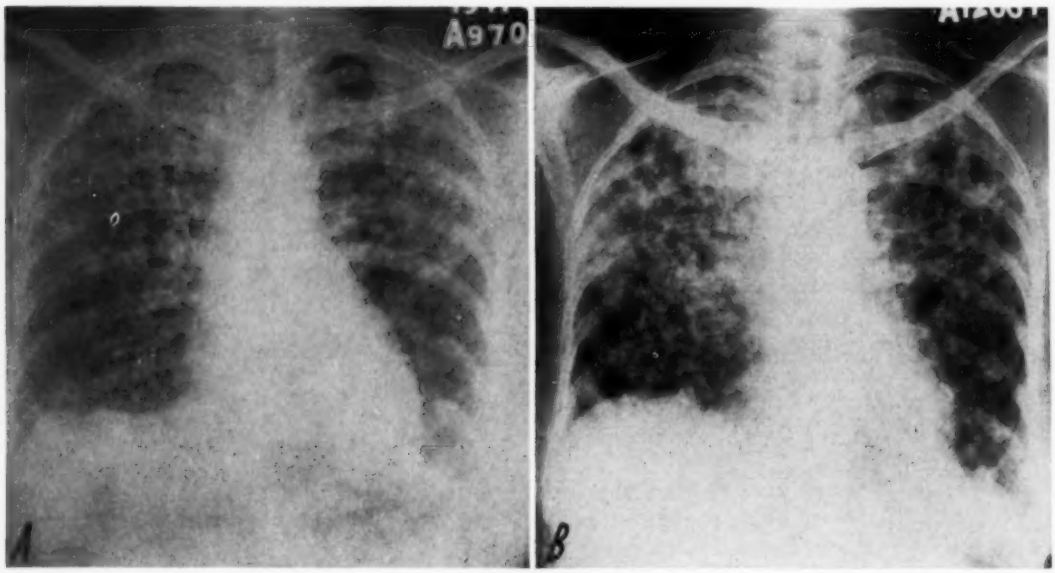

Fig. 2. Case II. *A*, roentgenogram of the chest taken September 16, 1941. *B*, roentgenogram taken on November 28, 1941. Comparison of these two roentgenograms shows the progress of the lesions and their tendency toward confluency.

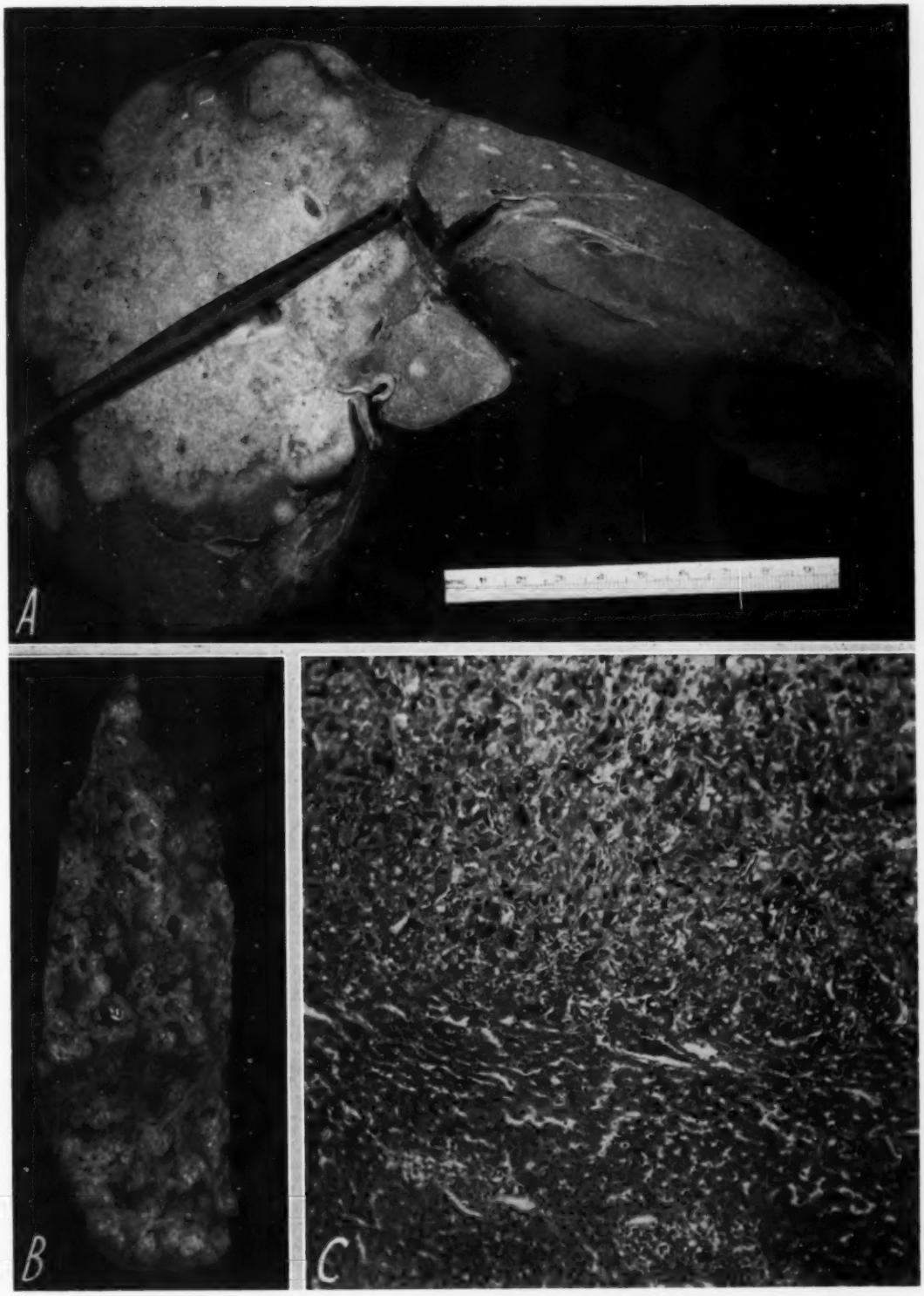

Fig. 3. Case II. *A*, cut section of liver showing massive involvement with metastatic tumor. Clamp holds vein apart at point of invasion by the new growth. *B*, portion of lung showing the character of the metastatic nodules. Several exhibit central necrosis. *C*, photomicrograph of section of lung.

Operation. October 10, 1941. Exploratory laparotomy—high right rectus incision. Firm carcinomatous mass was felt in the region of the gallbladder neck and cystic duct. A large gallbladder was opened and a large amount of thick mucopurulent exudate was removed. Biopsy was taken from the region of the cystic duct. The gallbladder was drained.

Course. Following surgery the patient's wound healed well. However, her course was progressively retrogressive and she died on December 29, 1941.

Pertinent Autopsy Findings. Prosector—Dr. Everett Wesp. Primary adenocarcinoma of the gallbladder with extension to the liver, common and cystic ducts and the peritoneum. The liver was enlarged and contained many cherry to plum-sized metastatic nodules and one huge conglomerate metastasis in the superior portion of the right lobe. This huge nodule showed central necrosis and definite invasion into the veins.

All lobes of the lungs had an almost solid infiltration of innumerable pea to bean-sized metastatic nodules, some showing central necrosis. The nodules contained a large amount of stringy mucoid material similar to that noted in the primary tumor. The tracheobronchial lymph nodes did not show metastases.

CASE III. B. T., male, white, aged forty-five, admitted to the hospital on December 1, 1941. For seven years prior to admission the patient had had a very suggestive peptic ulcer history with several instances of hematemesis. He had been in the hospital in November, 1940, following a rather severe gastric hemorrhage at which time a roentgen diagnosis of benign ulceration high on the posterior wall was made. The chest was roentgenoscoped during this same examination and no gross abnormalities were noted. Ulcer therapy was instituted and after a period of about one month the patient was discharged from the hospital with condition markedly improved. Red blood count and hemoglobin were at normal levels at the time of discharge. The patient was symptom free at discharge and until two months prior to his last admission when he developed anorexia and a feeling of fullness in the epigastrium. Food and alkalies were only of slight value in the relief of symptoms. A few weeks after return of abdominal complaints the patient began to experience dyspnea associated with paroxysms of coughing, both of which symptoms had progressed up to the time of admission. He had lost 20 pounds in weight during this same period.

Physical Examination. Temperature 98° F; pulse 90; respirations 22. The patient showed moderate dyspnea even while at rest in bed. His chest showed a few crepitant râles in both bases. There was one small hard supraclavicular node on the left side which clinically was thought to be a Virchow's node. Otherwise, the physical examination was essentially negative.

Laboratory Findings. Red blood count and white blood count were within normal limits. Wassermann reaction was negative. Blood glucose, albumin and globulin were within normal limits. Blood calcium and phophorus were within normal limits. Blood phosphatase was not elevated. Sedimentation rate was 26 mm. corrected. Sputum examinations were negative for tubercle bacilli.

Roentgen Findings. Roentgen examination of the chest on December 16, 1941, showed diffuse infiltrative areas throughout both lung fields which appeared as a hematogenous distribution. These areas tended to become confluent near the hilar shadows and in the mid portions of the lung fields. The roentgen interpretation was miliary carcinosis. The stomach was examined two days later and showed almost complete obstruction at the mid portion of the stomach due to filling in of the lumen with what was obviously an extensive malignant process in the mid portion of the stomach. The extent of the lesion could not be determined due to the degree of obstruction.

Course. The patient's course in the hospital was progressively retrogressive and he died on December 25, 1941. It was impossible to obtain permission for an autopsy on this patient.

Comment. We have included this case as one of miliary carcinosis to the lungs from the stomach although we have no pathological material for confirmation. The roentgen findings in the stomach seem convincing enough for a positive diagnosis of a gastric neoplasm. The roentgenogram of the chest showed an even, diffuse distribution of infiltrative lesions which seemed to be quite typical of metastatic malignancy. The patient at no time during his hospital stay showed any evidence of an infectious process which might account for a miliary type pulmonary lesion. Also we know that one year previously the patient's chest was clear at least at roentgenoscopic observation. Considering the above facts, we think we are

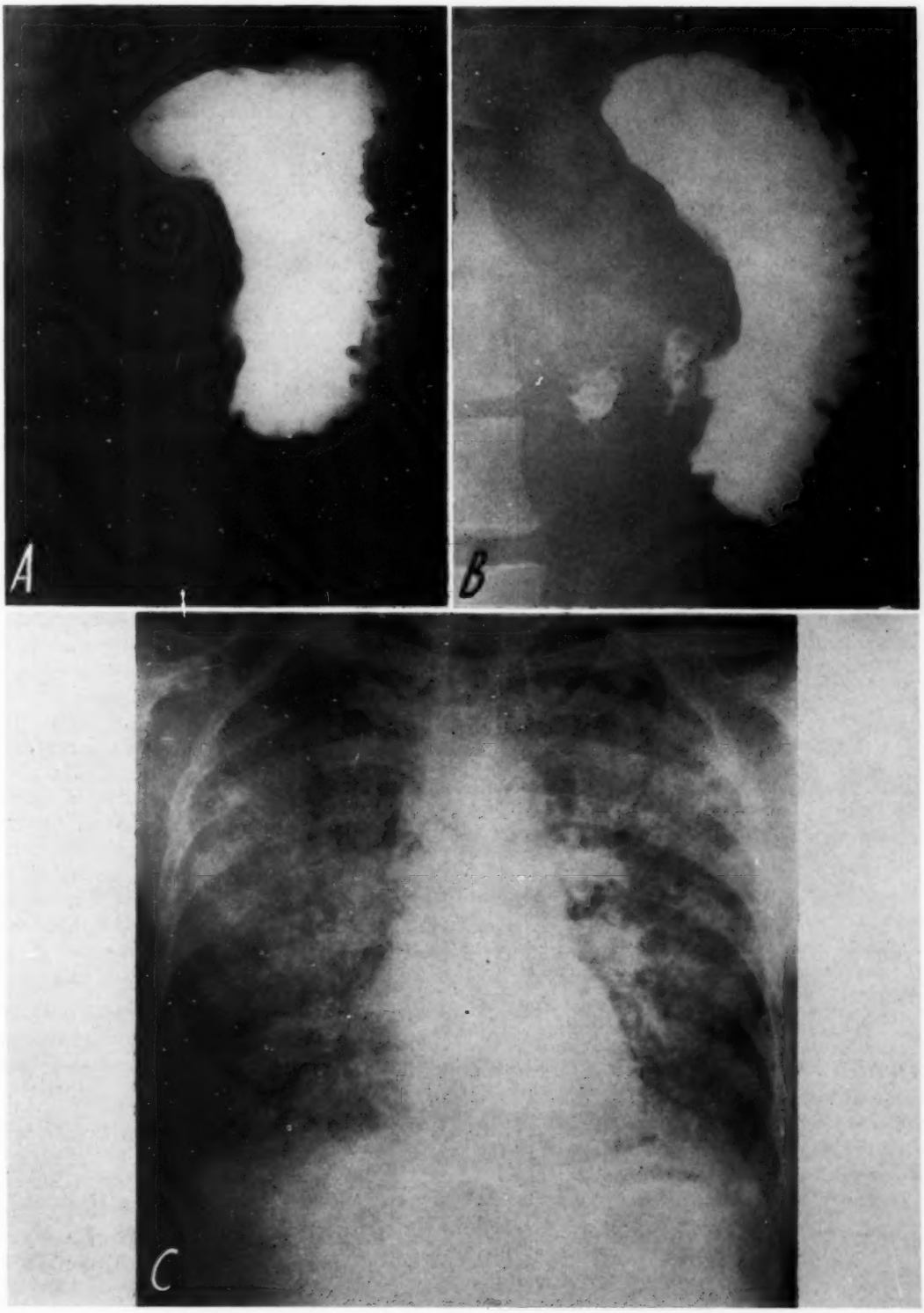

Fig. 4. Case III. *A* and *B*, roentgenograms illustrating the massive involvement of the stomach by new growth. *C*, roentgenogram of the chest.

justified in presenting this case as one of miliary carcinosis to the lungs from the gastrointestinal tract.

Case iv. E. T., male, white, aged sixty-two, admitted to the hospital on February 14, 1943. Three weeks prior to admission the patient developed some personality changes and complained of headache. He became progressively more drowsy and less cooperative and for the two weeks prior to admission was in a semicomatose condition.

Fig. 5. Case iv. Roentgenogram of the chest.

Physical Examination. Temperature 98° F.; pulse 48; respirations 20. The patient appeared semistuporous and followed directions hesitantly and incorrectly. He was dehydrated and his skin and mucous membranes were pale. Eyes: nystagmus to the left. Chest: some depression of breath sounds throughout the right chest otherwise negative. Neurological: reflexes were hyperactive. There was some motor weakness in the left arm and hand.

Laboratory Findings. Red blood count 3,360,000; hemoglobin 80 per cent; white blood count 16,600; Wassermann reaction negative.

Roentgen Findings. Skull: no abnormalities. Chest: evenly distributed mottled densities were scattered throughout both lung fields. They varied from pin-head to pea size. Their distribution was that of a hematogenous spread. The interpretation was probable miliary carcinosis. Ventriculogram: both lateral ventricles were dilated. The posterior horn of the right was obliterated and the body of the ventricle was depressed. Both right and left lateral ventricles were shifted to the left. The third ventricle was visualized and shifted to the left. The fourth ventricle was not filled. Interpretation: space filling lesion in the right occipitoparietal area. Possible second lesion in the subtentorial region as evidenced by lack of filling of the fourth ventricle.

At operation on February 15, 1943, ventriculography and biopsy of right occipitoparietal tumor were done. Examination of biopsy showed metastatic papillary mucoid carcinoma.

Course. The patient did not regain consciousness following surgery and died five hours later.

Pertinent Autopsy Findings: Prosector—Dr. Kornel Terplan. Primary walnut-sized gelatinous carcinoma of the head of the pancreas with metastatic carcinoma in several mesenteric nodes. Diffuse metastatic carcinoma of both lungs with multiple lentil to pea-sized nodules uniformly distributed through all lobes along with some recent edema and pneumonic congestion. Metastatic carcinoma of all bronchomediastinal nodes. Scattered metastatic nodules throughout the liver. Metastatic carcinoma in the medulla of the right adrenal. Metastatic nodule in the right parieto-occipital area of the brain. Huge metastatic lesion in the right cerebellar hemisphere measuring 5 by 5.5 cm. One hazelnut-sized metastatic nodule in the left cerebellar hemisphere. Extensive metastatic carcinoma of the supraclavicular lymph nodes bilaterally.

DISCUSSION

From a study of the 4 cases reported above, certain points may be stressed which aid materially in making a diagnosis of pulmonary miliary carcinosis. The chest roentgenogram is in many respects quite characteristic:

1. The lesions are evenly and diffusely distributed throughout both lung fields such as we would expect with a hematogenous spread through the pulmonary circulation.

2. The various lesions are not of homogeneous density but appear as soft mottled areas with fuzzy, poorly defined margins.

They usually exhibit a moderate variation in size. The variation may be from a diameter of 1 or 2 millimeters up to over a centimeter. As the disease progresses, there may be some confluency of the lesions.

3. Hilar node involvement from secondary lymphatic spread may or may not be present.

The differential roentgen diagnosis usually involves only two other conditions:

1. *Miliary tuberculosis*—the distribution is the same. However, the lesions are usually more discrete and of a more uniform size. Also the individual lesions have a more homogeneous density. The above, combined with the clinical evidence of infection noted in miliary tuberculosis, usually makes the differential diagnosis relatively easy.

2. *Silicosis*—in silicosis the mid lung fields exhibit the greatest degree of involvement in contradistinction to the even distribution seen in miliary carcinosis. Silicotic nodules appear hard, discrete and of quite uniform size. Also there is usually an associated peribronchial fibrosis and large dense hilar shadows. Secondary emphysema is also apt to be present in silicosis. The history of dust exposure and the clinical course are both helpful in establishing the correct diagnosis.

It is interesting to note the lack of physical findings in the chest in miliary carcinosis. In spite of the extensive pulmonary involvement in some of the cases presented, the positive physical findings were minimal to absent. It may be important to stress this fact as a negative finding. That is, the absence of physical signs in the chest would tend more toward than against a diagnosis of miliary carcinosis in the presence of suggestive roentgen findings.

It is of some interest to comment on the type of spread to the lungs noted in the 4 cases presented. Cases I and II showed primary cancer of the gallbladder with secondary invasion of the liver both by direct extension and by circulatory spread. The subsequent massive pulmonary involvement resulted from invasion of liver veins followed by the release of showers of tumor emboli to the right heart and the pulmonary circulation. These 2 cases are excellent examples of the second method for production of pulmonary miliary carcinosis outlined previously.

Case IV is an example of the first method outlined for production of miliary carcinosis. In this case the primary lesion was in the pancreas with secondary lymphatic spread. Spread to the supraclavicular nodes was probably by the thoracic duct which could also release a shower of tumor emboli to the right heart circulation. The second method of pulmonary spread must also be considered in this case because of the metastatic nodules in the liver. However, there was no pathologic evidence of invasion of the hepatic veins.

The pulmonary involvement in Case III is also probably best explained by spread along the thoracic duct, particularly in view of the presence of a typical Virchow's node. Of course, lack of pathologic data makes it impossible to rule out liver involvement.

Thus in at least 3 of these cases we can trace rather well the pathogenesis of the pulmonary lesions.

CONCLUSIONS

1. Miliary carcinosis of the lungs is not common but when it occurs it is important that the condition be recognized.

2. Certain conditions are necessary for such a spread of cancer since this type of spread must necessarily be hematogeneous through the pulmonary circulation.

3. Four cases have been presented and the pathogenesis of the pulmonary lesions traced.

4. The chest roentgenogram exhibits a fairly typical appearance which has been described.

5. Miliary tuberculosis and silicosis must be considered in the differential diagnosis.

6. The lack of physical findings in spite

of a marked degree of pulmonary involvement has been stressed.

7. A correlation of all available data on a single case will usually make the diagnosis of miliary carcinosis obvious.

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Vol. 54, No. 5

DIAPHRAGMATIC HERNIA AND DILATED ESOPHAGEAL AMPULLA*

THEIR CLINICAL AND DIAGNOSTIC SIGNIFICANCE

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THE number of cases of diaphragmatic hernia and dilated esophageal ampulla diagnosed roentgenologically has markedly increased. From a fraction of 1 per cent seen about two decades ago, we have reached the high figure of over 10 per cent of those cases presented for gastrointestinal roentgenological study. In our last 200 gastrointestinal examinations we encountered 23 cases of either diaphragmatic hernia or dilated esophageal ampulla. This is because the clinician and roentgenologist now routinely look for these conditions during such examinations.

Although the diaphragmatic hernia and the dilated esophageal ampulla are lesions of two different organs of the digestive tract, they have, nevertheless, many similar characteristics. Therefore, a roentgenologic differential diagnosis is at times difficult. For this reason the two subjects are combined in this presentation, describing their similarities and differences.

The most prevalent diaphragmatic hernia is the para-esophageal hiatus type (Fig. 1). The esophageal hiatus is located in the muscular part of the diaphragm and is surrounded by additional fibers derived from the crura of the diaphragm to form a sphincter. The distal end of the esophagus is normally closed at the hiatus by the hiatal sphincter and opens synchronously with deglutition. After middle age the muscles surrounding the esophageal hiatus tend to become atonic producing a dilatation of the hiatus. The increased intra-abdominal pressure resulting from constipation, flatus, pregnancy, etc., causes the fundic portion of the stomach to herniate through this enlarged hiatus, to enter the posterior mediastinum and lie alongside the esophagus, thus forming a para-esophageal hiatus hernia. The distal end of the esophagus is not disturbed by the hernia. It remains attached to the diaphragm.

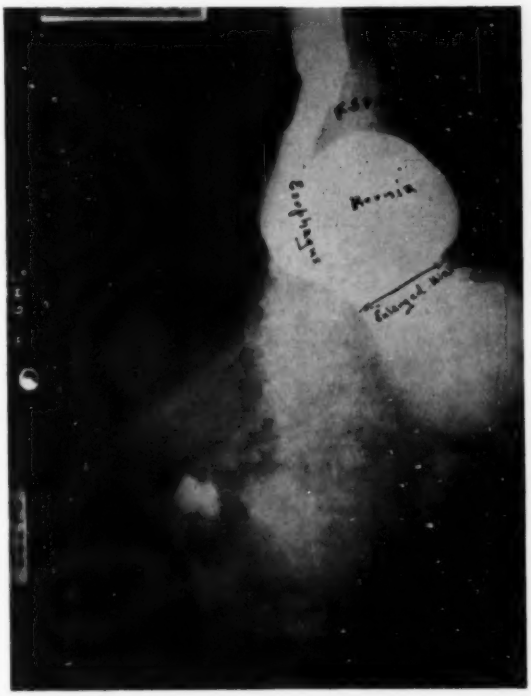

FIG. 1. Para-esophageal hiatus hernia. The esophagus is displaced laterally, and alongside the hernia.

In this position and when dilated, the hernia may produce pressure in the posterior mediastinum simulating symptoms of heart disease, or it may compress the esophagus, producing dysphagia. A very large hernia, by its bulk, can produce dyspnea and also displace the esophagus to the right of the midline. Often a bleeding ulcer is formed at the isthmus between the hernia and the

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Fig. 2. Para-esophageal diaphragmatic hernia, with a large ulcer at the isthmus between the stomach and the hernia, at the hiatus. This could be mistaken for a diverticulum of the stomach, except that the clinical symptoms were characteristic of a gastric ulcer.

stomach due to the constriction produced by the hiatal sphincter (Fig. 2).

Another type of hiatus hernia is that associated with the upward displacement of the esophagus (Fig. 3). During the protrusion of the stomach through the hiatus it carries the distal part of the esophagus into the mediastinum, freeing it from its attachment to the diaphragm, thus causing it to become tortuous and curved. These curves and tortuosities differentiate this type of hiatus hernia from the congenital, short esophagus type. These hiatus esophageal hernias are operable.

ENLARGED ESOPHAGEAL AMPULLA—PSEUDO-HERNIA

The esophageal ampulla has received little attention in medical textbooks. Mention is made on this subject for the first time in the 1936 edition of Cunningham's Anatomy,[1] as follows:

Immediately above the level at which the esophagus passes through the diaphragm there is a fusiform expansion of the tube, of variable length and girth, which has been called the ampulla phrenica, or esophageal ampulla. It lies in the lowest part of the posterior mediastinum, where the anterior wall is formed by the sloping posterior part of the diaphragm. Should the esophagus be obstructed at its passage through the diaphragm this ampulla may undergo great distention, and swallowed food may be retained in it and not pass on into the stomach.

Practically all the dilated esophageal ampullae (Fig. 4) that we have observed were due to spasm of the hiatal sphincter or spasm of the esophagus. This dilatation of the ampulla is most likely due to the effort of the esophagus to overcome the spastic obstruction, formed by the hiatal sphincter of the diaphragm. Similar ampullary dilatations in other parts of the gastrointestinal tract are encountered, as, for example, dilatation of the antrum pylorica, when the pyloric ring of the stomach is partly ob-

Fig. 3. Diaphragmatic hernia, with an upward displacement of the esophagus. Note the characteristic tortuosity of the distal end of the esophagus.

structed, or dilatation of the rectal ampulla, when the anal sphincter undergoes obstruction.

On several occasions during roentgenoscopy, formation of the ampulla and spasticity of the esophagus were observed. It was noticed that while the patient was drinking the barium mixture the hiatal sphincter, which normally opens and closes intermittently during deglutition, remained closed longer than usual. The lower 2 inches of the esophagus dilated, forming an ampulla, and an annular contracture formed at the upper end of the ampulla. Spastic ripples appeared around the walls of the ampulla and extended into the tube above it. The annular contracture deepened and finally closed the lumen completely. For a short time the ampulla was closed at both ends. During this time the intra-ampullary pressure increased to such a degree that it overcame the resistance of the hiatal sphincter; the latter opened and the esophageal contents emptied into the stomach, then the esophagus assumed its normal shape. Upon being questioned, the patients stated that the sensation was the same as that experienced during an attack of pain involving a wide area embracing the lower thorax and upper abdomen. Occurrence of such pain makes the patient seek medical aid.

Fig. 4. Enlarged esophageal ampulla. Note the constriction at the distal end of the ampulla, due to spasticity of the esophagus.

DISCUSSION

A dilated ampulla or a hiatus hernia may or may not produce local pain or tenderness. When symptoms are present they are of two types. One is produced directly by the lesion, in which case the usual complaints are dyspnea, prostration, bloating, pressure in the precordial region and shortness of breath. These symptoms are aggravated by a heavy meal or when the patient is in a recumbent position, because the stomach contents then easily regurgitate into the hernia or ampulla. However, when the stomach is partly filled with gas or air, as in aerophagia, the symptoms become aggravated even in the erect posture.

In the second type are symptoms referred to different parts of the body as the external ear, lower jaw, left shoulder and arm, precordium, and occasionally to the region of the gallbladder. The reason for this wide distribution of referred pain becomes obvious upon consideration of the complex nerve supply of the esophagus, diaphragm, and fundus of the stomach. All of these parts are supplied by branches of the upper cervical nerves, the recurrent laryngeal, vagus nerve, the sympathetic nervous system, and the phrenic nerve. We have had patients who were treated for cardiac conditions, chiefly coronary disease, and were confined to bed until a gastrointestinal examination revealed either a diaphragmatic hernia or a dilated ampulla. Harrington[2] states that many of his hernia cases were referred to him with a previous diagnosis of cardiac condition, gallbladder disease or peptic ulcer. Some came to him following surgery which had offered no relief.

The diagnosis of these conditions can be made by roentgenography or esophagoscopy. Either method may fail occasionally

to detect the lesion on primary examination. A second or even a third examination may be necessary to establish the diagnosis. The reason is that the condition is intermittent in character, the hernia often reducing itself, or the spasticity of the ampulla being relieved, freeing the patient from symptoms for days or even weeks. However, when adhesions form and the hernia remains permanently in the mediastinum the symptoms are constant.

TECHNIQUE

The technique for the roentgenographic demonstration of these lesions consists in increasing the intra-abdominal pressure during roentgen-ray exposures. This may be accomplished by placing the patient in supine position and applying direct pressure over the abdomen with an inflated rubber balloon, or by having the patient flex his thighs over his abdomen at the same time raising the shoulders and taking a deep breath.

DIFFERENTIAL DIAGNOSIS

The dilated esophageal ampulla must be differentiated from the following conditions:

1. Diaphragmatic hernia.
2. Cancer of the esophagus or cancer of the pars cardia of the stomach, invading the esophagus by continuity.
3. Cardiospasm.
4. Obstruction due to swallowing of a caustic substance.
5. Diverticula of the esophagus at the cardiac end.
6. Tumors originating in the adjacent organs that invade, or produce pressure on, the esophagus.

The diaphragmatic hernia, especially the para-esophageal type, can be recognized by the fact that it is situated alongside the esophagus above the diaphragm, and both the esophagus and the hernia can be seen separately on the roentgenogram. The ampulla, on the other hand, is in continuation with the esophagus. In the hernia with the upward displaced esophagus, the esophagus enters the hernia at its summit; the distal end of the esophagus assumes a characteristic twist (Fig. 3).

In cancer of the esophagus, a filling defect of the esophagus with an irregular outline, is present.

In cardiospasm, strange as it may seem, there is no spasm in the esophagus or in the hiatus. Cardiospasm is a misnomer. Hurst's[3] conception is that the hiatus is normally closed and is supplied by two sets of nerves: the sympathetic and the vagus. The sympathetic nerves keep the hiatus closed, while the vagus causes it to open. The pathology lies in the inability of the vagus nerve to cause relaxation and opening of the hiatus. He terms it "achalasia"—that is, inability to relax. The distal end of the esophagus in these cases is fusiformly dilated, smooth in outline, with no evidence of spasm. The lumen is uniformly enlarged. The swallowed food accumulates in the esophagus and opens the hiatus by its gravity when the food reaches a certain height in the esophagus. In the dilated esophageal ampulla, on the other hand, spasm is always present either in the ampulla or in the esophagus above it.

SUMMARY AND CONCLUSION

Acquired diaphragmatic hernia and dilatation of the esophageal ampulla are relatively common conditions. They are capable of producing symptoms almost perfectly simulating those produced by grave disease of the thoracic or upper abdominal viscera. Routine search for these conditions during gastrointestinal series will not infrequently give an explanation for the hitherto unexplained complaints. It is also suggested that patients with atypical angina pectoris, particularly if the pain is related to meals, be given the benefit of roentgenologic study before a diagnosis with such a severe prognosis be regarded as established.*

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CHRONIC NONSPECIFIC REGIONAL ENTERITIS*

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THE YEAR 1932 marks an important landmark in the progress of medical science, for in that year our knowledge of the diseases of the small bowel was greatly advanced as a result of the painstaking work of Crohn, Ginzburg and Oppenheimer.[1] In a paper published in the *Journal of the American Medical Association* these authors described, in its pathological and clinical details, a disease of the terminal ileum affecting young adults chiefly, and characterized by a subacute or chronic necrotizing inflammation, the cause of which was unknown.

Following the above announcement, reports of similar cases began to appear in the literature with ever increasing numbers up to the present day. New facts were discovered about the disease, viz., it was found that the affection is not always limited to the terminal ileum, but may involve any part of the small bowel and at times even the large bowel; it was also found that the lesion was not always continuous but was often interrupted by healthy segments of intestine. Because of the above findings the terms regional or terminal ileitis are gradually giving way to one which is more inclusive, viz., chronic nonspecific regional entertis, which is the title of the present discussion.

Previous to 1932 only a few sporadic cases had been reported, and hardly any before World War I. Was the disease nonexistent before the war or had surgeons and pathologists failed to recognize this affection? It hardly seems reasonable to believe that a disease with such gross manifestations would have failed to attract attention. It is more likely that the disease was very rare before the war for some unexplainable reason. Perhaps the great influenza epidemic then prevalent may have been in some degree a causative factor in bringing about an increase in the incidence of the disease.

The marked increase in this form of enteritis is well illustrated by the following statistical study. Brown and Donald[2] of the Mayo Clinic report that there were only 2 cases in 1922 and no others until 1929. Twenty-four instances of the condition were encountered prior to 1933, and during the past four years there have been 114 patients diagnosed as having this disease entity. Reports by other observers reveal the same tendency, namely, a constant increase in the frequency of the disease.

The pathological manifestations of the disease most often affect the terminal ileum but no part of the small or large bowel is exempt. Several of our cases showed definite involvement of the head of the cecum in addition to the ileum. In 1 case there were several areas of the disease process throughout the course of the colon. In another case extensive involvement of the duodenum was demonstrated four years after resection of the terminal ileum for regional ileitis. The latter case showed internal fistulous tracts extending from the diseased segment into the surrounding tissues.

The pathological process is characterized by a subacute or chronic necrotizing ulceration on a granulomatous basis. This results in a cicatrizing inflammatory process which is sharply localized. The intestinal wall is stiffened, becomes rigid, and the lumen is narrowed, resulting at times in a stenosis with dilatation of the proximal portion of the bowel. If the diseased process is not arrested or removed, perforation may take place with a resulting fistula or abscess formation. Very frequently the diseased segments of the bowel are matted together by

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dense adhesions giving the impression of a tumor in the right lower quadrant of the abdomen. Four of our cases presented large palpable masses which were thought to be due to new growths until their true nature was recognized by operation. The neighboring glands are usually found to be enlarged and the mesentary is edematous.

So far the cause of the disease remains unknown. According to Strömbeck[3] the disease strongly resembles a healed tuberculous ileitis. He is of the opinion that the process may actually be due to a tuberculous infection and advances the following reason, namely, the terminal loop of the ileum is well equipped to combat infection, therefore chances for a tuberculous infection to heal are good. Hence, if healing does occur, a microscopic picture may arise which is identical with that described by Crohn in terminal ileitis. Roentgenologically, Strömbeck believes that chronic terminal ileitis cannot be differentiated from ileocecal tuberculosis. Contrary to the above opinion the great majority of observers are of the opinion that the disease is caused by some other type of infection. One of the main arguments against a tuberculous origin is the rarity with which pulmonary tuberculosis is found associated with regional ileitis while it is very commonly associated with tuberculous ileitis. Not one of our cases showed the slightest evidence of pulmonary tuberculosis.

There are no pathognomonic signs or symptom-complex in regional ileitis which would lead the clinician to arrive at a correct diagnosis, but those which are present are strongly suggestive of an intestinal disturbance. There are abdominal pains which are cramp-like in nature and usually limited to the right lower quadrant. Diarrhea is a frequent symptom with the stools containing mucus and sometimes blood. There is also evidence of a low grade infection, such as loss of weight and strength, fever and occasionally a leukocytosis. On physical examination tenderness is often elicited upon pressure in the right lower quadrant and occasionally a palpable mass may definitely be outlined. Four of our cases exhibited palpable masses in the right lower abdomen.

The diagnosis of the disease can only be established by a thorough investigation of the small bowel. The roentgen method has proved to be the most useful method for this purpose, provided it is carefully carried out. This entails frequent observation of the barium column from the moment it leaves the stomach until it reaches the large bowel, which is then examined by means of a barium enema. When the examination is carried out as above directed the chances are very good of recognizing any organic lesion of the small and large bowel.

The roentgen signs depend upon the gross alterations of the bowel as a result of the pathological changes. In the order of importance and frequency they are as follows:

1. Deformity of the contour of the bowel wall.
2. Narrowing of the lumen of the intestinal tube.
3. Loss of the mucosal pattern.
4. Hour-glass constrictions in the course of the bowel.
5. Rigidity and immobility of the involved segment.
6. Displacement of adjoining segments of the bowel as a result of pressure by pseudo-tumors.
7. Demonstration of internal fistulous tracts.
8. Hypermobility of the intestinal contents.
9. Stenosis with dilatation of the proximal portion of the bowel.

There are several conditions from which chronic nonspecific regional enteritis is to be differentiated.

1. *Chronic Appendicitis.* Most of the cases referred for roentgen examination have a clinial diagnosis of possible chronic appendicitis. Roentgen examination may not establish the diagnosis of chronic appendicitis but it can, at least, exclude regional ileitis. The presence of an appendiceal abscess may be readily diagnosed by

the history of the onset and the absence of intestinal involvement.

2. *Tuberculous Ileitis.* The roentgen appearance of regional ileitis very frequently resembles that of tuberculous ileitis, but the absence of pulmonary tuberculosis, the almost constant accompaniment of the latter, will exclude it.

3. *Colitis.* Colitis is confined to the colon alone. The small bowel is seldom involved, while in regional ileitis the colon is rarely affected without the small bowel also being involved.

4. *Small Bowel Tumors.* Malignant tumors seldom occur in the small bowel, but when they do they are usually localized. In regional ileitis the lesion is more extensive and may present normal bowel segments between the affected areas.

The above discussion is based upon the observation of 12 cases, 2 of which were discovered before 1932. In view of our present knowledge there is no doubt about the nature of the 2 cases, but instead of having called it regional or terminal ileitis it was then described as a chronic inflammatory process, of an undetermined etiology, of the lower end of the ileum.

In view of the fact that even now the exact cause of the affection is not known, the present terminology is little more explicit than the one used at that time.

Case 1. D. H., male, aged thirty, was seen in 1926. For over a year he had been troubled with pain in the abdomen, especially in the right lower quadrant. A mild degree of diarrhea was present. The physical examination revealed a well nourished young man with a palpable, tender mass in the right lower abdomen. The clinical diagnosis was chronic appendicitis, but roentgen examination showed a deformed terminal ileum and cecum which was very suggestive of a tuberculous ileitis (Fig. 1), but in the absence of pulmonary tuberculosis such a diagnosis was doubtful.

The patient was operated upon and according to the surgeon's report the lesion did not appear to be tuberculous in nature. The coils of the ileum were thickened and matted together giving the impression of a new growth.

Fig. 1. Case 1. Terminal ileum deformed and adherent. Cecum ill defined.

No attempt was made to remove the diseased bowel and the patient died of shock following the operation.

Case 11. R. W., female, aged twenty-five, married, was seen in 1927. For over a year and a half the patient had been troubled with more or less pain in the right lower abdomen. A mild form of diarrhea was present from time to time. Her general health remained fairly good. On physical examination a palpable tender mass was disclosed in the right lower quadrant. The clinical diagnosis was either chronic appendicitis or a new growth. Roentgen examination revealed a distorted terminal ileum with upward displacement of the cecum by the palpable mass (Fig. 2). The general good condition of the patient seemed to preclude a malignant growth, and the absence of pulmonary tuberculosis likewise favored the exclusion of tuberculous ileitis. She was given roentgen treatment and her condition improved, but after a year the symptoms returned and she was operated upon at the Mayo Clinic. A chronic process of the ileum, apparently not of a tuberculous origin and not due to a new growth, was found. Since then she has been operated upon several times for recurrences and at

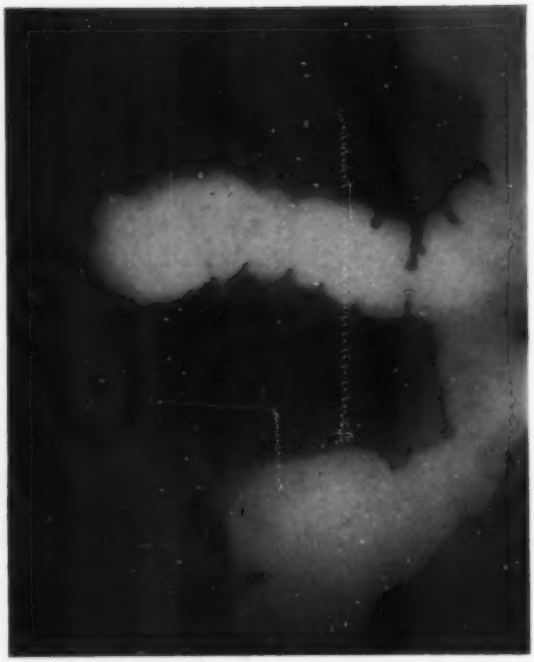

Fig. 2. Case II. Terminal ileum deformed. Head of cecum displaced upward by palpable mass.

present is, relatively speaking, in fairly good condition.

Case III. M. A., male, aged sixteen, was seen in January, 1935, because of abdominal cramps, loose watery stools, loss of weight and moderate fever. On physical examination a moderate degree of tenderness was elicited in the right lower abdomen. Roentgen examination revealed a deformed terminal ileum, with narrowing of the lumen and rigidity of the entire segment (Fig. 3). The diagnosis of regional ileitis was confirmed by operation at the Mount Sinai Hospital, New York.

Case IV. A. C., male, aged twenty-two, was examined in February, 1936, because of pain in the abdomen, a moderate degree of diarrhea and a mild fever. On physical examination tenderness, found in the right lower abdomen, was thought to be due to appendicitis. Roentgen examination revealed a deformed terminal ileum which was more or less fixed (Fig. 4). The diagnosis of regional ileitis was confirmed by operation at the Jewish Hospital. In January, 1943, seven years later, the patient returned because of a sensation of fullness, pain in the abdomen and diarrhea. Another roentgen examination showed a recurrence of the lesion in the segment of the bowel near the colonic anastomosis. The question of another operation was discussed, but neither the patient nor the surgeon was fully in favor of it so at my suggestion it was decided to use roentgen therapy. The reason for this suggestion was based upon the known fact that granulomatous lesions are often radiosensitive, and since ileitis consists of a granulomatous overgrowth, the possibility that it might favorably be influenced by roentgen irradiation appeared to be a logical conclusion. Therefore, a course of roentgen treatments was given, consisting of ten applications with the following factors: 200 kv., 8 ma., 0.5 mm. Cu plus 1 mm. Al filter, 50 cm. distance, 200 r to each of three fields, front, right side and back. In all he received 2,000 r over a period of twenty days. The symptoms gradually subsided and further roentgen examination showed a definite improvement in the local condition. Recently he was again examined and the lumen of the bowel was found to be definitely wider than before and his present condition is very good.

Fig. 3. Case III. Terminal ileum narrow and deformed. Defect in head of cecum.

Case v. J. W., female, aged nineteen, was examined in April, 1940, because of gas pains, loss of weight and strength, diarrhea and a moderate fever. The roentgenogram showed extensive involvement of the ileum and jejunum characterized by loss of the mucosal pattern, irregular contour, marked narrowing of the lumen, and immobility (Fig. 5). The diagnosis of regional ileitis was confirmed by operation at the Mayo Clinic. Notwithstanding the operation, the patient made poor progress and died in May, 1944.

Case vi. F. M., female, aged twenty-one, was referred in 1942 for roentgen examination.

Fig. 4. Case iv. Terminal ileum deformed and fixed.

because of pain in the right lower abdomen, fever and loss of weight. Roentgen examination revealed a deformed terminal ileum with a narrow lumen. The head of the cecum was found to be contracted and irregular in outline (Fig. 6). The diagnosis of terminal ileitis was confirmed by operation at the Jewish Hospital. The patient returned in May, 1943, with a recurrence of the symptoms, and a re-examination revealed involvement of the segment of the bowel near the anastomosis. A second operation was performed but recently she returned with the same complaints and the roentgeno-

Fig. 5. Case v. Extensive involvement of ileum which is narrow and deformed.

Fig. 6. Case vi. Deformed narrow terminal ileum.

Fig. 7. Case vii. Extensive narrowing of the lumen, which is fixed.

gram again revealed a new recurrence of the disease. Roentgen therapy was decided upon. The same factors as previously noted were given with the exception of the dose which was reduced to 100 r because of her small size and debilitated condition. In this case it is too early to draw any definite conclusions; however, six months after treatment she is symptom free and has gained 15 pounds in weight.

Case vii. S. B., female, aged fifty, the oldest patient in the series, was examined in May, 1942, because of pain in the abdomen, especially in the right lower quadrant. There were also nausea, vomiting and moderate fever. Roentgen examination disclosed an extremely narrow, ill defined segment in the region of the ileum which extended across the abdomen and was more or less fixed (Fig. 7). The diagnosis of terminal ileitis was confirmed by operation at the Jewish Hospital. Her present condition is good.

Case viii. M. H., female, aged twenty-one, was referred for roentgen examination of the gastrointestinal tract because of abdominal pain, moderate diarrhea with blood and mucus, loss of weight and strength. The symptoms have lasted about four years with periods of remissions. Of late she has also been troubled with nausea and vomiting. During examination of the stomach and duodenum the proximal jejunum was found to be dilated. This observation led to frequent examinations during the next seven hours. The later observations showed strictures in the bowel with segments presenting deformed contours encroaching upon the lumen of the bowel (Fig. 8). Twenty-four hours later the small bowel was found to be dilated with barium. The colon was filled, but without dilatation. Diagnosis of regional enteritis was confirmed by operation which consisted of an enteroenterostomy. Segments of both the jejunum and ileum were found to be involved.

Case ix. P. F., aged sixteen, was referred in October, 1942, for roentgen examination because of pain, tenderness in the lower abdomen and fever. Three hours after a barium meal the terminal ileum and cecum were partially filled. The ileum was interrupted by strictures with intervening dilated segments. A barium filled

Fig. 8. Case viii. Marked dilatation of segments of jejunum and ileum with intervening strictures.

string-like shadow connected it with the cecum (Fig. 9). On the following day the colon was found to be partially filled. A barium enema showed displacement of the sigmoid flexure to the left, apparently by a mass in the right lower quadrant. The head of the cecum was contracted and irregular in outline probably as a result of involvement by the same disease process. The diagnosis of regional ileitis was confirmed by operation at the Jewish Hospital. The operation consisted in a short-circuiting anastomotic procedure. The patient is now doing well.

Case x. F. W., female, aged twenty-eight, was referred in November, 1942, because of abdominal pain in the right lower quadrant where a tender mass was palpable. Four hours after a barium meal the terminal ileum and proximal portion of the colon were found to be partially filled. The barium in the ileum consisted of small dilated segments due to hour-glass constrictions and the whole was more or less displaced upward apparently by the palpable mass (Fig. 10). On the following day the small bowel was found to be empty and the colon partially filled. Barium enema revealed downward displacement of the sigmoid flexure and compression of the medial margin of the cecum and ascending colon by the palpable mass. The diagnosis of regional ileitis was made and confirmed by operation. The patient returned in July, 1944, with an external fistulous tract. Another operation, which consisted in a short-circuiting anastomosis procedure was performed. Her present condition is good.

Fig. 9. Case ix. Narrow terminal ileum with hour-glass strictures.

Fig. 10. Case x. Hour-glass strictures of terminal ileum.

Case xi. J. I., male, aged twenty-five, was examined in March, 1943, because of abdominal pain, diarrhea and loss of weight and strength. During a period of two years before the present roentgen study the patient was examined in several cities of this country but no definite diagnosis was made to explain the cause of his symptoms. The barium was injected through a Miller-Abbott tube and the ileum was found to consist of many irregular segments, some being dilated while others were more or less constricted and deformed (Fig. 11*A*). On the following day a barium enema revealed marked spasm of the cecum and ascending colon. Within that region a long linear shadow, apparently due to an internal fistulous tract, was recognized (Fig. 11*B*). After the spasm was relaxed and the colon was filled completely, several irregular translucent areas were noted in the cecum, ascending and transverse colon encroaching upon the lumen of the bowel and apparently due to masses of granulomatous infiltrations (Fig. 11*C*). The patient was operated upon and a good deal of the ileum and colon was resected. The diagnosis of a chronic non-

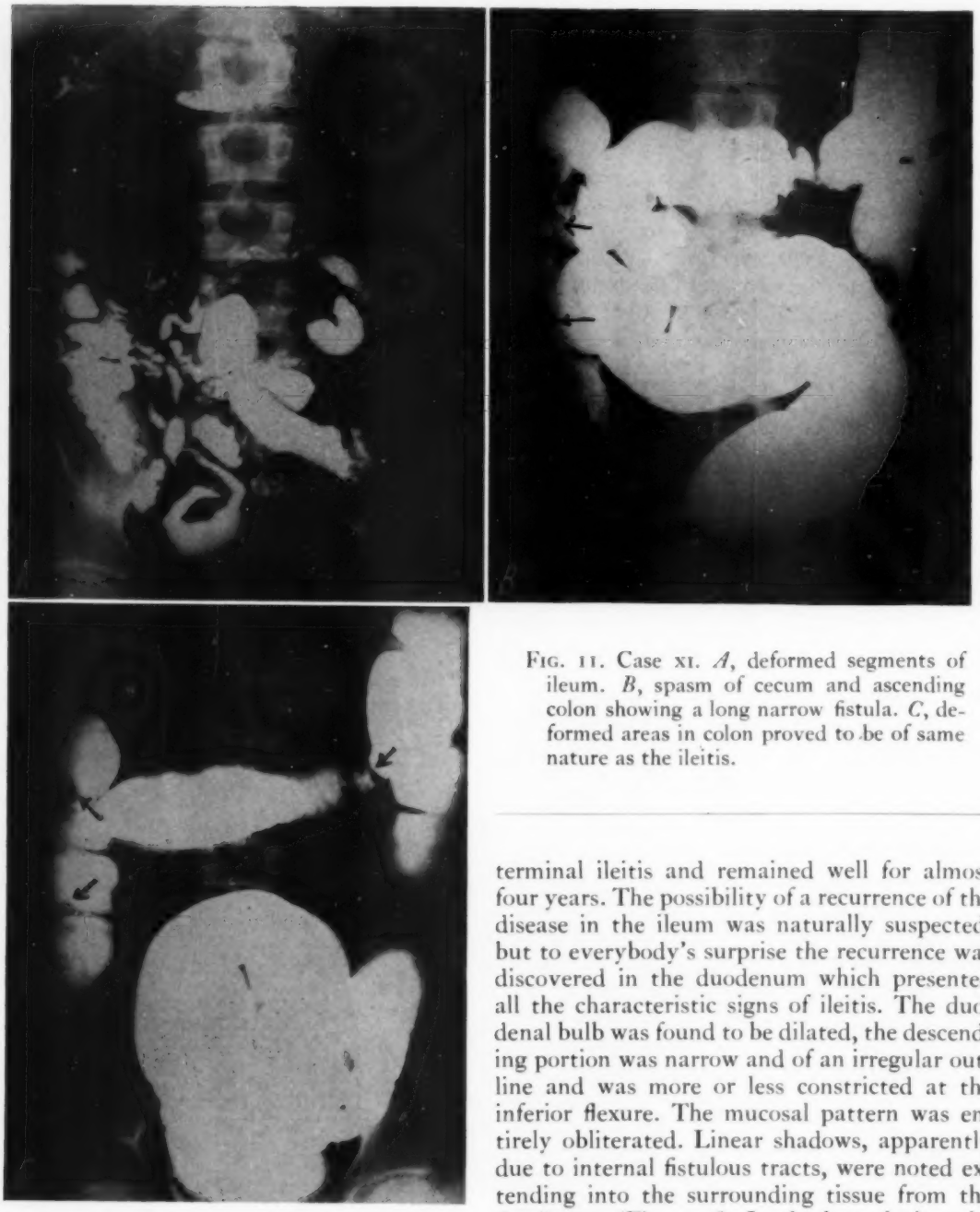

FIG. 11. Case XI. *A*, deformed segments of ileum. *B*, spasm of cecum and ascending colon showing a long narrow fistula. *C*, deformed areas in colon proved to be of same nature as the ileitis.

specific enteritis was confirmed. The patient's condition remains good.

CASE XII. P. W., male, aged twenty-nine, was referred for an examination in June, 1943, because of pain in the abdomen, diarrhea and moderate fever. In 1939 the patient had been operated upon at the Jewish Hospital for terminal ileitis and remained well for almost four years. The possibility of a recurrence of the disease in the ileum was naturally suspected, but to everybody's surprise the recurrence was discovered in the duodenum which presented all the characteristic signs of ileitis. The duodenal bulb was found to be dilated, the descending portion was narrow and of an irregular outline and was more or less constricted at the inferior flexure. The mucosal pattern was entirely obliterated. Linear shadows, apparently due to internal fistulous tracts, were noted extending into the surrounding tissue from the duodenum (Fig. 12*A*). In the lateral view the deformity and stricture of the duodenal wall was demonstrable to greater advantage (Fig. 12*B*).

The question of operation was given up and at my suggestion roentgen treatment was used. The technique was similar to that of the other male patient. The symptoms gradually receded, the patient gained weight (35 pounds)

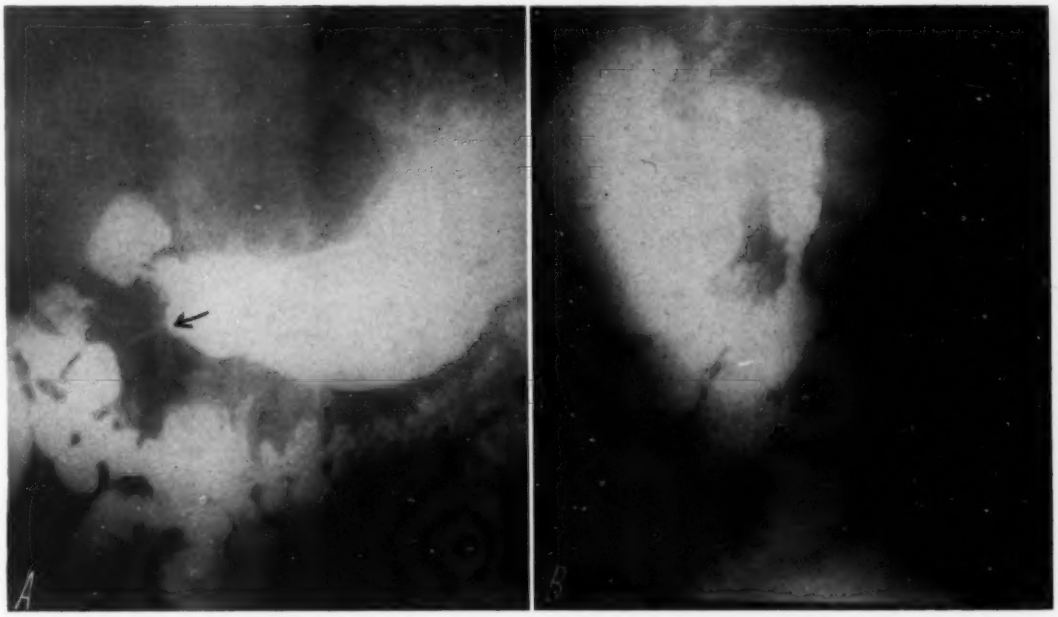

Fig. 12. Case xii. *A*, deformed descending duodenum with fistulae. *B*, lateral view. Duodenal constrictions shown to greater advantage in a case of regional ileitis.

and strength and has now been a full time employee for over a year and a half. Several reexaminations showed the lumen of the duodenum to be less constricted but the mucosal pattern has not fully recovered.

SUMMARY AND CONCLUSIONS

The discussion of chronic nonspecific regional enteritis is based upon the observation of twelve cases, two of which were diagnosed before 1932 which was the year Crohn and his associates reported a series of chronic inflammatory lesions of the terminal ileum.

An analysis of the clinical symptoms and physical signs exhibited by these cases reveal no symptom-complex pathognomonic of the disease. However, they are strongly suggestive of disease of the intestinal tract, a fact of much importance to the roentgenologist who is now taking greater pains in the examination of the small intestine.

Most of the lesions encountered were in the terminal ileum, but some cases showed involvement of the jejunum and duodenum The cecum was frequently found to be involved and in one case the greater part of the colon was extensively affected.

Recurrences are frequent and take place in the segment of the bowel nearest the anastomosis.

The diagnosis in all of the cases was established by roentgen examination and confirmed by operation. The roentgen signs in the order of importance are as follows: contour deformity, narrowing of the lumen, hour-glass constriction, loss of mucosal pattern, rigidity and immobility, internal fistulous tracts, malposition of neighboring intestine, hypermotility and stenosis.

The treatment in all cases was surgical. In three recurrent cases roentgen therapy was tried with remarkable results.

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DISCUSSION OF PAPERS BY DRS. ABOWITZ AND BROWN

Colonel B. R. Kirklin, M. C. I was rather interested in reading Dr. Abowitz's paper a few days ago to find that he states the incidence of hernia in his experience has been more than 10 per cent of cases examined. In our experience the incidence hasn't been nearly that high, but has been about 1.8 per cent.

One other feature of his paper in which our experience has been a little different is the incidence of para-esophageal hernia. Of the patients with diaphragmatic hernia that have been operated upon, we have found that only one-third had the para-esophageal type. On the true esophageal hernia which carries the esophagus up with it, we have no accurate statistics but it is my opinion that not more than 25 per cent of the hernias that we have seen have been of the para-esophageal type.

I am anxious to emphasize Dr. Abowitz's statement that the diagnosis of esophageal hernia is primarily roentgenologic. I am sure that 95 per cent of the hernias that are diagnosed at the Mayo Clinic are incidental roentgen diagnoses in the course of a routine examination of the stomach; that is, in at least 90 to 95 per cent of the cases, the clinician has not suspected the presence of a hernia.

Another thing that I would like to emphasize is that approximately 18 per cent of the hernias have a history of bleeding.

On the question of dilated esophageal ampulla, I am not just clear about what Dr. Abowitz means by this symptom or condition. It has been my opinion that there is considerable variation in the width of the lower esophagus and the esophageal ampulla in different individuals. Frequently we see what appears to be dilatation of the esophageal ampulla and upon questioning that patient, usually one past middle life, he will admit to being a rather fast eater; that is, he gulps his food rather rapidly. It seems reasonable to me to assume that that might be one of the contributing factors.

I feel that there is much variation in the width of the lower esophagus. Sometimes it is very difficult to differentiate the dilated ampulla from a very small esophageal hiatus hernia where we have just 1 inch or 2 inches of stomach protruding up through the esophageal hiatus.

In his paper, Dr. Brown developed a few points which seem to be worthy of special emphasis.

In the years elapsed since Crohn and his associates first called attention to the benign, non-tuberculous, subacute or chronic necrotizing and cicatrizing inflammatory intestinal process now known variously as regional enteritis or ileitis, hyperplastic ileitis or enteritis, ulcerohyperplastic enteritis and other similar descriptive names, much has been written and said about the disease, and opinions about practically all phases of it except its etiology are now fairly unanimous.

The roentgenologic descriptions seem, however, to have stressed that stage in the pathogenesis of the disease in which the involved portion of intestine is shortened and its lumen more or less markedly narrowed as a result of the thickening of the intestinal walls.

It is true that this is the most frequent roentgenologic manifestation of the disease but it is not the only one. The earlier in its pathogenesis the disease is encountered, the less markedly will contracting (narrowing—shortening) deformities of any kind be manifest.

In the early stages of the disease the lumen may not be perceptibly narrowed, shortening of the involved portion may not be obvious, and the roentgen diagnosis will be based on such evidence as relatively minor changes in the relief pattern of the mucous membrane, a sense of diminished pliability and mobility perceived by the palpating hand during the roentgenoscopic examination, both combined perhaps with a local or general intestinal hypermotility.

The greater the deformity, the more advanced is the disease, and such roentgenologic findings as stenosis with prestenotic intestinal distention, internal fistulae with peri- or paraintestinal abscesses, hour-glass constrictions and the formation of pseudo-tumors, all are to be considered, in my opinion, as evidence of advanced disease.

Dr. Brown has made a very competent analysis of the roentgenologic manifestations of nonspecific regional ileocolitis, and I would like to commend him for it.

We have been recommending surgical treatment in our cases with extirpation of the involved intestine as the ultimate aim. There have been recurrences, and the management of these often becomes a most trying problem. Dr. Brown's success with roentgen therapy in

at least 2 of his cases is interesting and encouraging. I do not know that roentgen therapy has been tried before, but I can think of no reason why it should not be tried, at least in selected cases.

We will all be interested in Dr. Brown's later experiences along these lines.

Dr. Abowitz (closing). The percentage does not seem so high when one considers that the two conditions, diaphragmatic hernia and esophageal ampulla, are grouped together. The reason for this grouping is that, at times, it is difficult to differentiate one condition from the other on the roentgenogram. The clinical symptoms are of little help, as they are almost identical in both cases.

As to the roentgenographic technique, two points must be stressed: (1) the intra-abdominal pressure should be increased during exposure; (2) the filled esophagus, and the hernia or ampulla, should be taken on the same film. This helps in making the correct diagnosis. Without a filled esophagus, it is at times difficult to recognize the type of lesion one is dealing with.

ROENTGEN EXAMINATION IN CONGENITAL INTESTINAL OBSTRUCTIVE DEFECTS IN INFANTS

ITS AID IN PLANNING SUITABLE SURGICAL APPROACH AND PROCEDURES FOR THEIR CORRECTION

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THE incidence of imperforate anus and atresia of the intestine of various types is variously placed at 1:8,000–1:10,000 (Keen[11]), 1:5,246 (Bardeleben[2]), 1:7,477 (Zimindorff[2]) and 1:11,000 (Kermisson[7]), 1:5,000,[8] newborn infants. From January 1, 1923, to December 31, 1944, there were 9,474 living babies born in the hospital of St. Vincent de Paul and De Paul Hospital. Among these only 2 cases of obstructive congenital intestinal anomalies have been recorded. The condition is thus relatively infrequent, but obviously intelligent correction is of utmost importance. The purpose in presenting these cases is (*a*) to emphasize the importance of early examination to determine the site of obstruction, and (*b*) to draw particular attention to important details of roentgen technique, with special reference to imperforation and atresia of the anus and rectum.

The site of obstruction depends upon the stage at which embryological development has become erratic. Briefly stated, the development of the lower intestinal tract is as follows: In the embryo the urinary tract and the lower intestine at first are one cavity. This cavity becomes divided into anterior and posterior portions by the urogenital membrane—the anterior chamber becomes the bladder and the posterior forms the rectum or mesenteron. The mesenteron descends toward the perineum where it meets an infolding epiblast (proctodeum) which becomes the anus. Malformations in this region are due to failure of the urogenital membrane to separate completely the rectum from the bladder or failure of the proctodeum to meet and unite with the mesenteron. Drueck[6] states that the arrest in imperforate anus is usually at the level of the peritoneal reflection; in females it is usually about 2 cm. and in males it is usually about 3 cm. from the perineum. The atresia may thus be complete (imperforation) or fistulous (atresia), and anomalous openings may be present anywhere between the rectum and the urogenital tract.

Keiller,[7] in 1924, appears to have been the first to recognize the value of roentgen examination in these cases. He advised the use of the roentgen ray "if available," and if sufficient gas had formed, but he did not give details of technique or show illustrations. He also appears to be the first to have used barium suspension injected through the colostomy opening to demonstrate the site of obstruction where surgical intervention from above had become necessary because of failure to locate the blind end of the rectum through the perineum. Desmarest and Ebrard,[5] in 1926, gave bismuth by mouth and made anteroposterior and lateral roentgenograms with an opaque object in the anal dimple.

In 1930 Wangensteen and Rice[12] described a method whereby gas contained in the large intestine was used to delineate the blind end of the rectal pouch. They showed that if the baby were suspended head down, the gas would rise to its highest point and that a roentgenogram made with an opaque object in the anal dimple would demonstrate the extent of separation between the blind end of the rectum and the perineum. The surgeon could then determine whether a perineal approach were feasible. Rhodes[10], in 1934, recommended

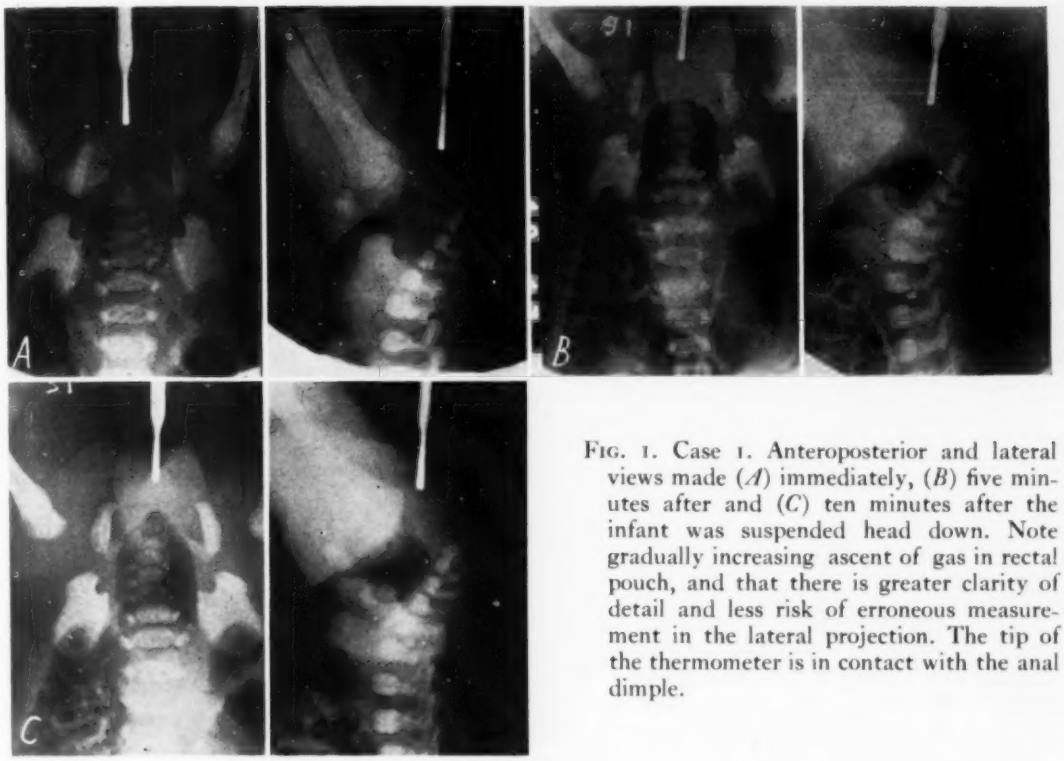

Fig. 1. Case 1. Anteroposterior and lateral views made (*A*) immediately, (*B*) five minutes after and (*C*) ten minutes after the infant was suspended head down. Note gradually increasing ascent of gas in rectal pouch, and that there is greater clarity of detail and less risk of erroneous measurement in the lateral projection. The tip of the thermometer is in contact with the anal dimple.

that the child be stimulated to cry, and buttermilk be given by mouth to obtain filling of the intestine with gas; thereafter, anteroposterior supine and lateral recumbent roentgenograms were made to determine the location of the blind end of the rectal tube.

Ladd and Gross,[8] while recommending the method proposed by Wangensteen and Rice, reported erroneous localization in 2 cases because of insufficient gas in the lower intestine. Berman[1] and Crowell and Dulin[4] drew attention to the possibility of error during the first twenty-four hours of life since gas is not normally present in the colon during the first day. Despite these objections, the method is the simplest devised, and accumulating experience shows it reasonably reliable. The method of Wangensteen and Rice is preferred to those in which the patient remains supine or recumbent since, in the latter, the gas is apt to remain proximal to the blind end of the rectum. Administration of opaque suspension by mouth is likely to cause obstruction of the large intestine.

CASE REPORTS

Case 1. W.E.B., a white male infant, about two months premature, was born after normal home delivery. The birth weight was 5 lb., 10 oz. and the infant appeared to be normal in all respects save that there was no anal orifice, though there was a dimple. He was admitted to the hospital nine hours and twenty minutes after birth. Both parents were healthy and there was no family history of malformations. Three, six and nine hours after admission he was given half an ounce of 5 per cent lactose by mouth for the purpose of obtaining an accumulation of intestinal gas. On one occasion, twenty-seven hours after birth, he vomited green liquid material. The morning following admission, and twenty-seven hours after birth, roentgen examination was undertaken.

Roentgen Examination. The infant was suspended head down before a loaded cassette and exposures were made in anteroposterior and lateral projections, with a thermometer tip held in apposition with the anal dimple. These

roentgenograms (Fig. 1*A*) showed the closed end of the large bowel approximately 2.5 cm. from the tip of the thermometer. It occurred to me that possibly sufficient time had not been allowed to elapse between inverting the baby and taking the roentgenograms. Therefore, two additional sets of roentgenograms were made at intervals of five and ten minutes after the infant had again been suspended head down (Fig. 1, *B* and *C*). It was found in the five minute roentgenogram that the distance between the blind end and the thermometer tip was approximately 1.5 cm., and in the ten minute roentgenogram 1.0 cm. It was further noted that more accurate measurements were possible from the roentgenograms made in lateral projection since, in the anteroposterior views, the pelvic curvature of the intestine gave an erroneously shorter distance.

Operation. Twenty-eight hours after birth an incision was made through the anal dimple and the blind pouch was encountered about 1 cm. above the cutaneous margin. The pouch was isolated, partially freed, and brought down through the opening in the dimple. It was opened and the edges of mucosa were sutured to the skin. No anesthetic was used.

The postoperative course was uneventful and five hours after returning from the operating room the infant had a large meconium stool. He was discharged from hospital the day following operation and since then has shown normal development. Slight anal tightness was overcome by occasional dilatation.

Case II. B., a white male infant, born at term, birth weight 7 lb., 3 oz. The infant was apparently normal except for the fact that the anal orifice was defective; it consisted of a pinpoint opening to the left of the median raphe, with no corresponding opening on the right side. A slight amount of meconjum was expelled through this orifice twenty and three-quarter hours after birth, but it was not possible to insert a small catheter or the tip of a thermometer through it. There was no vomiting. Twenty-one and one-half hours after birth the infant was referred for roentgen examination. He did not receive any lactose solution to aid in the formation of intestinal gas.

Roentgen Examination. There was a pinpoint opening to the left of the median raphe but attempts to introduce the tip of a syringe, a fine catheter and to inject iodized oil were unsuccessful. Roentgenograms made in anteroposterior and lateral projections at intervals up to ten minutes after the baby had been suspended showed the minimum distance between the gas distended rectal pouch and anal orifice to be about 1 cm. In this, as in the previous case, roentgenograms made at earlier intervals showed a greater separation between the gas and cutaneous marker.

Operation. A grooved director was inserted through the pin-point opening and the median raphe was cut. When this was done, the anal canal appeared to be normal except that it was rather small.

The postoperative course was good. The earlier stools were of meconium; later they became normal and the baby was discharged with its mother on the eighth post-partum day.

Comment. These cases demonstrate the importance of waiting a sufficient length of time after inverting the infant before taking roentgenograms. Ten minutes is probably not too long; a shorter length of time is likely to give an erroneous impression. They also illustrate the superiorty of lateral roentgenograms over those made in anteroposterior projection, although both projections should be utilized since the lower end of the rectal canal may be displaced laterally. Contrary to the views of Berman[3] and Crowell and Dulin[4] the time of adequate intestinal gas accumulation cannot be set abitrarily at twenty-four hours since in Case II examination was less than and in Case I only slightly greater than that interval.

Case III. B., female infant, was born, about seven months' gestation, of healthy parents. Her birth weight was 5 lb., 2 oz. She was born at 4:45 A.M. and at 7:00 A.M. there was projectile vomiting of meconium-like material. During the subsequent eighteen hours the vomiting continued. Saline enemas were returned clear, but she could tolerate only about an ounce of solution and they were immediately and forcibly expelled. The fact that a rectal thermometer could be inserted for a distance of only 3 to 4 cm. led to the clinical impression that she had a rectal atresia and she was referred for roentgen examination twenty-eight hours after birth.

Roentgen Examination. The technique of examination was the same as for the cases recorded above. A small catheter was inserted into the anus to a distance of about 3.5 cm., and there appeared to be a rather wide separation between it and the gas-distended rectal pouch in the roentgenograms made ten minutes after the infant had been suspended head down (Fig. 2*A*). This suggested the possibility of a high imperforation of the rectum. For the purpose of more accurately defining the respective blind ends, approximately 15 cc. of air was injected by syringe through the catheter. Contrary to expectation, no gas escaped from the anus and in roentgenograms immediately afterward, the rectum, sigmoid and large intestine could be defined (Fig. 2*B*). Thereafter injection of 15 cc. of iodized oil showed clearly that there was no atresia of the large bowel below the region of the left upper quadrant (Fig. 2*C*). There was slight filling of what was taken to be the distal half of the transverse colon, though it was displaced laterally by a large cystic mass medial to it. The descending portion of the colon had a redundant loop and it was thought that there had been a failure of descent of the cecum. There was a slight accumulation of gas in the small bowel. The following morning the infant was examined again by plain roentgenograms without additional contrast medium (Fig. 2*D*). The large intestine was visualized by gas content in the right upper quadrant and it ended in close proximity to the cyst-like mass. Both the blind end of the intestine and the cyst had been displaced, between the times of examination, from the left to the right upper quadrant. At this time it was also noted that there was marked gaseous distention of the stomach and loops of small intestine. On the basis of these findings it was thought that there was an obstruction of the small intestine, probably in the region of the terminal ileum.

The infant's condition gradually became worse and was very poor when operation was undertaken on the same day as the second roentgen examination. The roentgen impression was confirmed: there was a blind termination of the ileum several centimeters from the proximal end of the colon, and they were joined by a fibrous band. The closed end of the colon was found under the liver but more extensive exploration with reference to the cyst-like mass was not possible because of the infant's poor condition. She did badly after operation and died about sixty hours after birth.

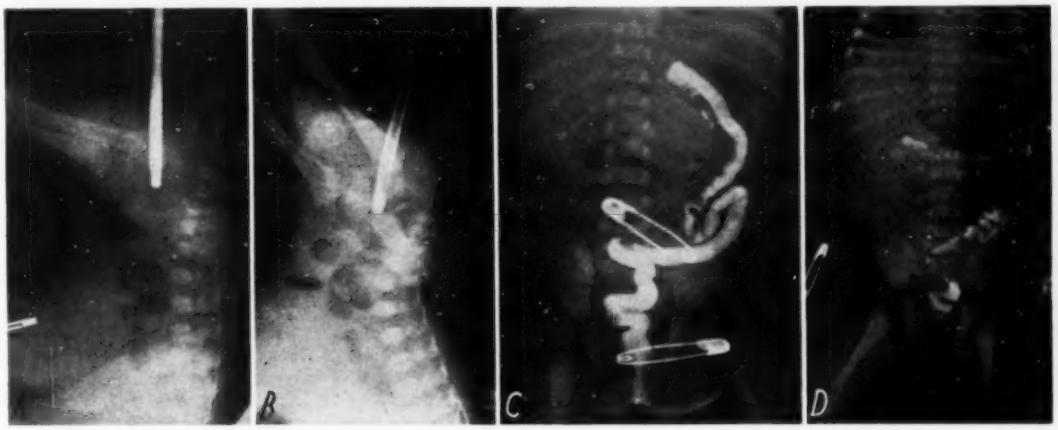

Fig. 2. Case III. The findings in (*A*), reproduced from a roentgenogram made ten minutes after the infant was suspended head down, show evidence suggestive of high rectal imperforation. This was disproved by insufflation of air (*B*) and injection of iodized oil (*C*). The partially calcified enterocyst is seen in (*C*) and (*D*) in close proximity to the mobile proximal end of the colon.

Autopsy. At autopsy the cyst-like mass seen in the roentgen studies was found to be a partially calcified enterocyst below the hepatic fissure. It contained brownish material resembling fecal matter, and was connected to the terminal ileum by a fibrous strand and to the mid-ileum by an almost atretic loop. Bands of fibrous adhesions connected it to both right and left lobes of the liver and to the

omentum. The ileostomy was wide open and there was no obstruction between it and the proximal small intestine and stomach.

Comment. It appeared feasible to demonstrate the depth of the anal or rectal atresia, using insufflation of air in the anal pouch as contrast medium. The injected air was successful in ruling out the presence of obstruction of the anal canal, rectum and large intestine; this was confirmed by use of opaque medium. An impression of small, rather than large, intestinal obstruction was confirmed at operation. The enterocyst and proximal end of the large intestine were apparently freely movable since between examinations they changed from the left to the right side. This case illustrates the importance of using contrast medium to demonstrate accurately the depth of the anal pouch.

SUMMARY

1. Three cases illustrating congenital obstructing anomalies of the intestinal tract in newborn infants have been presented and details of the technique of roentgen examination have been described. It is believed that proper roentgen examination can be of great aid in guiding the surgical approach.

2. Roentgen examination, to be of value, should be made after the infant has been suspended for at least five, and preferably ten minutes head down, in order to obtain maximum ascent of gas in the blind rectal pouch.

3. Where there is no anal opening, an opaque object should be held in apposition to the site of the dimple. If there is an anal pouch, opaque medium should be injected into it. These measures will permit an accurate estimate of the depth of tissue between the anal membrane or perineal surface and the blind end of the rectal pouch.

4. Roentgenograms made with the patient suspended head down in lateral projection are of greater value in estimating the thickness of tissue between the rectal pouch and the perineal skin surface, since the pelvic curve of the intestine gives an erroneously short distance between these points when viewed only in anteroposterior projection. However, the anteroposterior view is important to demonstrate possible deviation to left or right of the terminal end of the rectum.

The author desires to acknowledge his indebtedness to Drs. E. D. Floyd, N. F. Mullen and B. Steingold, attending physicians, and to Dr. C. C. Smith who operated upon all three patients, for permission to use these cases.

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Vol. 54, No. 5

THE SO-CALLED FIFTH AND SIXTH CEREBRAL VENTRICLE*

A CLINICAL AND ROENTGENOGRAPHIC STUDY AND CASE REPORT

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INTRODUCTION

THE correct diagnosis of some of the less frequently occurring cerebral lesions was greatly facilitated and, in many instances, made possible for the first time by Dandy's[1,2] discovery of ventriculography and pneumo-encephalography in 1918 and 1919. Prior to that time, most of these disorders were recognized mainly during postmortem examinations.

To these rare conditions of the central nervous system belong the rather heterogeneous group of true cysts. They should be distinguished from the large division of cyst-like formations or false cysts which arise from various causes as from parasitic maladies, degenerative changes in tumors or tumor-like granulomatous disease processes, interference with the flow of blood through the cerebral vessels, traumatic effects, and other obvious reasons. Sometimes, differentiation may be very difficult as, for example, in those cases where ependymal adhesions snare off portions of the ventricles, converting them into cyst-like structures. Very often, microscopic examination of the walls of the cysts is necessary to differentiate between true and false cysts.

Among the interesting anomalies of development of the region of the septum pellucidum, the corpus callosum and the fornix, rather frequent sites of malformation as described by Jaeger and Bannwarth,[8] Reeves,[11] Love, Camp and Eaton,[10] and Thompson,[13] are the cysts which are caused by the pathological enlargement of the slit between the laminae of the septum pellucidum and the space between the undersurface of the corpus callosum and the psalterium or lyre of David underneath, both perhaps better known as the fifth and sixth ventricle. The knowledge of this subject is by no means new, only the recognition during life is of recent origin. The cavum of the septum pellucidum has been known to anatomists for at least two centuries. Regarding the sixth ventricle, Andrea Verga, an Italian anatomist of the nineteenth century, claimed to be the first to describe this anomaly. Since then it has been called Verga's ventricle or cyst of Verga, although it is sometimes also known as the ventricle of Strambio, the ventricle of the fornix and the triangular ventricle. In 1931, Dandy[3] first evaluated the ventriculographic appearance and clinical symptomatology of these anomalies. To him should also go the honor for the first surgical attempt based upon a correct clinical diagnosis. The proper diagnosis is of importance because of the fair possibility of surgical correction in favorable instances, and because the recognition and separation of the asymptomatic types may avoid unnecessary surgical procedures.

ANATOMY

In most textbooks of anatomy, the cavum of the septum pellucidum and the cavum of Verga are mentioned only briefly, the former more extensively discussed than the latter, and the same is true in textbooks of pathology, regarding their hydropic alteration. However, it would be erroneous to conclude from this that they are extremely rare. According to Dyke[5] these developmental anomalies occur singly

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or in combination once in every three hundred persons.

The cavum of the septum pellucidum is usually referred to as a cystic or hydropic enlargement of the potential space between the leaves of the septum pellucidum which, lying in close apposition, but none the less being separated from each other, form the medial partition of each anterior horn and

FIG. 1. A coronal section of the brain through the region of the cerebral peduncles, showing a cavum of Verga. The tip of the probe points to one distinctly visible wall.

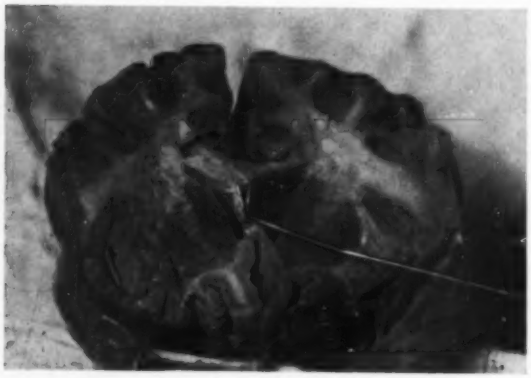

FIG. 2. A frontal coronal section of the same brain, showing a co-existing cavum of the septum pellucidum. The tip of the probe enters the lower portion of this cavum.

adjacent portion of the body of the lateral ventricle, and simultaneously the lateral boundary of the fifth ventricle. The anterior wall consists of the undersurface of the genu and the adjoining part of the corpus callosum. The posterior boundary is formed by the anterolateral surface of the columns of the fornix, the floor by the anterior commissure and the rostrum of the corpus callosum, while the roof is produced by the frontal portion of the body of the same structure. The cavum lies in the median sagittal plane, its main axis having a vertical direction.

Caudally to the cavum of the septum pellucidum and also approximately in the same plane lies the cyst of Verga occupying the space between the undersurface of the corpus callosum and the top of the psalterium, a commissural structure between the rhinencephalic pathways in the fornices. The posterior boundary of this cavum is contributed by the bulge of the splenium of the corpus callosum, and the anterior wall is formed by the limbs of the fornix. The structure has a triangular shape and flares out to either side, following for a short distance the curved course of the fornices (Fig. 1 and 2).

Dandy[3] states that both ventricles coexist and, in most instances, also coalesce, both cysts appearing as one large cavity. The point of coalescence is occasionally conspicuous by a more or less marked narrowing or actual constriction that bears resemblance to an aqueduct-like structure. These communicating cysts are frequently associated with developmental anomalies of the fornices. The cavum of Verga may exist on one side of the midline only; the other alluded half may be absent or a potential space.

The fifth and sixth ventricle may be completely isolated from the surrounding regular ventricular system, constituting a closed type of cystic enlargement. However, this occurrence is infrequent, for they are usually connected through various openings with the third and lateral ventricle. These openings are inconstant in location, shape and size, very often being subdivided by threads of tissue. The most frequently encountered names for them are the foramen of Mihalkowski and the valve of Vieussens.

Dandy[3] advises against the use of the term ventricle because their embryological development is entirely independent and also different from the anlage of the

regular ventricular system. According to Hochstetter,[6] a process of absorption within the originally solid leaf of the septum pellucidum is supposed to convert this structure into two parallel laminae with either a potential or cystic space between them. In contrast to it is the origin of the regular ventricular system which arises from the original neural tube by a process of evagination. Dandy[3] also points to the fact that the so-called fifth and sixth ventricle are conspicuous by the complete absence of choroid plexus in their wall.

PHYSIOLOGY

Being considered as developmental anomalies, no physiological importance is attached to their existence. However, a great deal of study has been devoted to the origin of the fluid in these cysts. It is obvious that the instances with communication into the regular ventricular system contain cerebrospinal fluid. In cases without any communication, the mode and site of production of the fluid is without satisfactory explanation, and, so far, only theoretical speculations have been offered instead. Some authors were of the view that a transudate from the third or lateral ventricle constituted the main source of the fluid. Van Wagenen and Aird[14] objected, basing their argument against it on the sometimes considerable thickness of the wall of these cysts which is incongruous with the suspected mechanism of transudation into the cysts. Wolf and Bamford[15] tried to find ependymal cells in the lining of the cysts as a plausible source. However, they and other authors alike did not find such cells in the wall, it being composed mainly of glial fibers with a moderate number of interlaced fibrillary astrocytes. None the less, they admitted that the presence of aberrant or greatly modified ependymal cells with secretory properties could not definitely be ruled out.

It is also rather surprising that there is no adequate chemical analysis. In his report on the chemical analysis of the contents of 56 cerebral cysts, Stern[12] did not mention even one of the congenital type. The explanation for this may perhaps be found in the technical difficulties which are encountered during the surgical exposure since, as a rule, blood is mixed with the fluid.

PATHOLOGY

Van Wagenen and Aird[14] divide the cysts of the fifth and sixth ventricle into two main groups, the communicating and non-communicating, the latter being subdivided into the primary and acquired variety. This division is based mainly on the observation that the non-communicating type may give rise to clinical symptoms; the other variant remains asymptomatic in most instances.

In the primary non-communicating type, no openings have ever been established since their first embryological appearance. They remain completely isolated from the adjacent regular ventricular system. This group is seemingly extremely rare. According to Dyke,[5] only one case has been observed among 4,000 pneumo-encephalographic examinations. As a rule, the non-communicating cavity changes into a communicating cyst because the steadily growing intracystic pressure causes breaks in the wall with the establishment of fistulous openings into the adjacent third or body of the lateral ventricle. From this type arises the secondary or acquired non-communicating division whenever obliteration of the once produced communication reconstructs the continuity of the wall. This mechanism is mainly the result of changes associated with universal or partial hydrocephalus, causing hydrops of the fifth and sixth ventricle alone or in association with dilatation of the regular ventricular system.

Both variants of the closed type may give rise to clinical syndromes by blocking the outlet of the third ventricle, the foramina of Monro or perhaps both, producing an internal hydrocephalus and increasing the intracranial pressure. These

cysts may also exert direct pressure upon the adjacent solid neural structures, especially the corpus callosum which becomes flattened and atrophied. It is also easily understood how intermittency of the deleterious effect produced by these cysts may ensue, simply by cyclic changes from the non-communicating to the communicating and again back to the closed variety.

The differentiation between the closed and open type is easily made by careful air studies of the intracranial content. If the air appears simultaneously in the cysts and also in the regular ventricular system, this is sufficient proof of free communication. However, careful consideration should be given to the possibility that the alteration of the intracranial pressure, associated with and following the drainage of the cerebrospinal fluid, may have reopened otherwise obliterated fistulae or set in motion a ball valve-like mechanism. In favorable instances, a permanent opening may be established in this manner and a curative effect obtained. In view of these possibilities, it is advisable to repeat the roentgen examination after twenty-four, forty-eight or more hours in order to study the behavior of the air in the cysts in comparison with the regular ventricles. Air may remain trapped within the cysts at a time when the other ventricles have already partially or completely regained their roentgenographic opacity. This is evidence of an unstable communicating system. An associated considerable thickness of the wall may also be contributory to retarded absorption of air.

CLINICAL SIGNS

It has only recently been pointed out that clinical manifestations may be produced by these hydropic anomalous ventricles, especially by the closed type. However, in no reported case was the symptomatology characteristic enough to permit a correct diagnosis with a fair degree of accuracy.

Hitherto published reports revealed the presence of mental and neurological disturbances. The fact that Verga's cases were inmates of psychiatric institutes is perhaps more than just a curious coincidence. However, there are also many descriptions where these cysts have been found during postmortem examinations of mentally and neurologically normal persons.

Neither the mental nor the neurological signs are in any way specific. The neurological syndromes are usually referable to the sequelae of increased intracranial pressure with its well known subjective and objective manifestations. Convulsions have been reported. Should the corpus callosum be sufficiently damaged, the somewhat vague syndrome that is associated with such a location of the lesion may dominate the clinical picture. Even less specific than the neurological symptoms are the mental signs, resembling psychoneurotic features in many instances. Perhaps the intermittency of the clinical signs and also the long duration are worthy of consideration. It is obvious that the differential diagnosis, from a clinical point of view, without the aid of roentgenographic air studies, offers great difficulties.

THE ROENTGENOGRAPHIC APPEARANCE AND ITS DIFERENTIAL DIAGNOSIS

A plain anteroposterior and lateral roentgenogram of the skull will hardly give evidence as to the presence of these cysts because the specific weight of their content does not materially differ from that of the surrounding neural structures and the cerebrospinal fluid, thus affording neither obstacle nor facilitation for the penetration of roentgen rays. Under extraordinary circumstances one may suspect the presence of these cysts on plain roentgenograms if there should show up some incidental calcification of either the wall, content, or perhaps both. On an anteroposterior view of the skull, such calcification may easily be confused with

and can hardly be differentiated from other calcifications in a similar location as, for instance, from calcareous deposits in the pineal gland or in the course of the choroid plexus of the third ventricle, or from partially calcified tumors of the midline. A lateral view offers the same differential diagnostic difficulties. From the foregoing, it may be concluded that only air studies afford sufficient security in the establishment of a correct diagnosis.

Air studies of cases with the closed type of cysts of the cavum pellucidum will reveal on a good anteroposterior roentgenogram a dense, rounded shadow between the air-filled anterior horns and the frontal portion of the body of the lateral ventricles with their gaseous content affording a sharp contrast. This rounded shadow separates the leaves of the septum pellucidum, bulging each one toward the lumen of the anterior horns in a more or less symmetrical way. On the lateral view, this shadow may not become discernible for because of its smallness it is easily extinguished by the subtraction effect of the air in the regular ventricles which, being projected upon each other, reinforce the phenomenon of subtraction. A coexisting Verga's cyst may be diagnosed by its mechanism of displacement which depresses and distorts the roof and body of the third ventricle, and also by the appearance of an internal hydrocephalus, as has been pointed out in the preceding pages. A coincidentally calcified pineal gland may also be displaced downward and posteriorly. In pneumo-encephalographic studies with visualization of the corpus callosum, a thinning of this structure may also appear. Concerning the differential diagnosis, tumors arising from the septum pellucidum or the anterior portion of the falx have to be distinguished from the cysts of the closed type lying between the leaves of the septum pellucidum. Regarding the differential diagnosis of the closed type of the cyst of Verga, tumors of the third ventricle and of the pineal gland closely resemble the roentgenographic appearance of Verga's cavum.

In contrast to the difficulties encountered in recognizing the closed cysts is the ease with which open types are visualized on an anteroposterior roentgenogram. However, this direction alone does not permit the recognition of a co-existing sixth ventricle because they lie in the same plane and are consequently superimposed. Their co-existence is at once discovered on an additional lateral view. Here in turn, a co-existing cavum pellucidum may not show up for the same reason as has been discussed regarding the closed type. The cyst of Verga is easily seen as an oblong shadow of least density, its top usually appearing somewhat below the upper boundary of the nearby ventricular body and its floor slightly lower than the bottom of the same structure. This appearance is based on the anatomical peculiarity of the corpus callosum which, narrowed down to a small fascicle in the midline, lies here nearer the

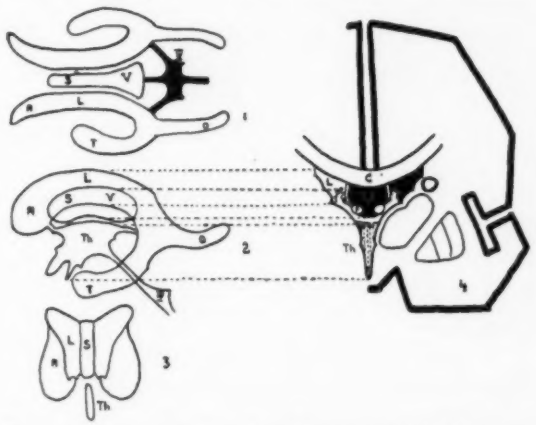

Fig. 3. Schematic drawing demonstrating the topographic relationship of the cyst of the cavum of the septum pellucidum and cavum vergae. *1*, view of the ventricular system from above; *2*, lateral view of the ventricular system; *3*, frontal view of the ventricular system; *4*, coronal section through the brain at about the mid-region of the body of the lateral ventricle; *A*, anterior horns; *C*, corpus callosum; *F*, fornix; *L*, lateral ventricle; *O*, occipital horns; *S*, cyst of cavum of septum pellucidum; *T*, temporal horns; *Th*, third ventricle; *V*, Verga's cyst; *IV*, fourth ventricle.

base of the skull than laterally where it diverges upward forming there the roof of the lateral ventricle. On the other hand, the floor of the cyst of Verga rests upon the psalterium, just above the tela choroidea of the third ventricle and the tectum of the midbrain, these structures being higher compared with the floor of the ventricular body (Fig. 3).

As both cysts co-exist in practically all instances, they cause on the lateral view the appearance of a comma-shaped shadow, with its longest axis oriented in the rostrocaudal direction. This comma-shaped shadow may show a slight constriction near the center, indicating the point of union.

Although the isolated occurrence of a Verga's cyst without the cyst of the cavum pellucidum has been denied by Dandy,[3] this anomaly by itself has also been reported. Leslie[9] observed such an instance and he tried to coordinate his exceptional case with Dandy's statement as to the contrary. Leslie speculated on the possibility that a co-existing cyst of the septum pellucidum was present at an earlier period, but because it became obliterated later, gave the impression of an isolated Verga's cyst in this particular case.

Regarding the differential diagnosis of the roentgen findings in the communicating types, agenesis of the corpus callosum may produce a similar appearance. Hyndman and Penfield[7] studied these cases and gave a detailed description of their roentgenographic appearance. In cases with congenital agenesis of the corpus callosum, the roof of the third ventricle reaches upward to the undersurface of the falx which, in some instances, actually indentates the top of the third ventricle which is also broader than usual. While the third ventricle is extending upward, it comes to lie between the anterior horns and adjacent portions of the lateral ventricles, pushing these structures to either side. Furthermore, the absent corpus callosum causes a batwing-like outline of the lateral ventricles on an anteroposterior view. This and the already mentioned imprint of the roof of the third ventricle by the falx are characteristic enough to permit a differential diagnosis between agenesis of the corpus callosum and communicating hydrops of the cavum pellucidum on an anteroposterior roentgenogram. On a lateral view, the cyst of Verga may be separated from the upward extending third ventricle in congenital agenesis of the corpus callosum by the presence of a line of demarcation which indicates the bottom of the cyst of Verga and the roof of the third ventricle, this demarcation being absent in agenesis of the corpus callosum.

CASE REPORT

Mrs. W. B., housewife, white, aged twenty-five, was admitted to the neurological service of the Jefferson Hospital for the relief of headache and convulsive seizures. Since about her twelfth year of life she had been suffering from this diffuse headache, which came in bouts and was frequently associated with nausea and occasional vomiting. Very often, her headache was accompanied by general aching, and occasionally it occurred without other symptoms. Of late, these episodes of headache appeared closer together and were getting progressively worse. At no time did she ever experience any double vision, motor or sensory impairment. She also complained a great deal of nervousness, inability to concentrate and forgetfulness.

For the last five or six years she had also been suffering from episodes of unconsciousness for which she had no recollection. However, her immediate relatives reported generalized jerking of arms and legs during the state of unconsciousness. They also observed bluish discoloration of the face and adjacent blush zone prior to the onset of the convulsive phenomenon. Tongue biting was also noticed. The patient never lost urine or stool during the convulsions. The convulsive seizures lasted for several minutes and were always initiated by loss of posture and groaning. No abnormal subjective sensation preceded the convulsions. Afterwards, the patient was comatose and later disoriented. This confusion wore off gradually over a period of several hours and severe headache followed. Prior to the onset of

the headaches and convulsive seizures, the patient was healthy. Her family history was also essentially negative and non-contributory.

The physical and neurological examinations were essentially negative. The analysis of blood and urine did not reveal any abnormality. The spinal fluid was clear, colorless and under normal pressure. The chemical, serological and cytological examination of the spinal fluid was negative. Following the spinal puncture, her

Fig. 4. Anteroposterior view of skull with air in the ventricles. Between the anterior horns the two leaves of the septum pellucidum are seen. They enclose a communicating type of cyst of the septum pellucidum.

symptoms became worse; a drawing sensation appeared in the nape of her neck, and she complained of seeing every object "four times," one behind the other one.

In view of the severe headache, a ventriculogram was made and the following roentgen findings were obtained: On the anteroposterior view of the skull (Fig. 4), a cavum pellucidum

Fig. 5. Lateral view of skull with left side away from film. Roentgenogram was taken immediately after trephining for ventriculography. A comma-shaped shadow appears. The arrow points to the junction of the two cysts.

became visible. On the lateral view (Fig. 5 and 6) a cyst of Verga appeared, both anomalies being united and forming an oblong comma-shaped shadow of least density with a slight constriction at the point of coalescence. The diagnosis of a congenital hydrops of the fifth

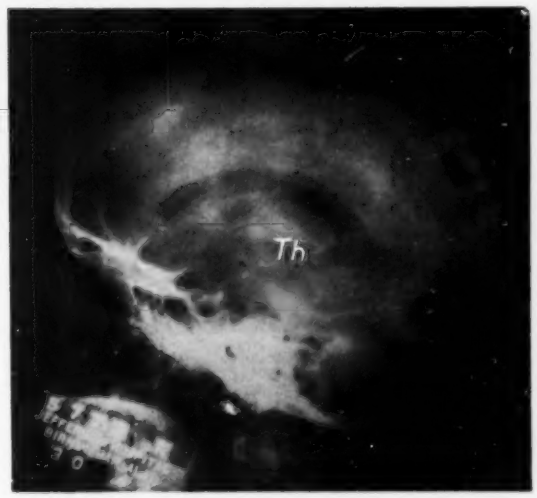

Fig. 6. Same view but with right side away from film. The comma-shaped shadow is distinctly visible, its bottom being sharply demarcated from the roof of the third ventricle. *Th*, third ventricle.

and sixth ventricle was made. The presence of air in these cysts proved a free communication. Additional air studies were taken at twenty-four, forty-eight and sixty-two hours following the trephining for ventriculography (Fig. 7). From these studies it became clear that the absorption of the air in these cysts was somewhat delayed in comparison with the regular ventricular system. This finding would suggest

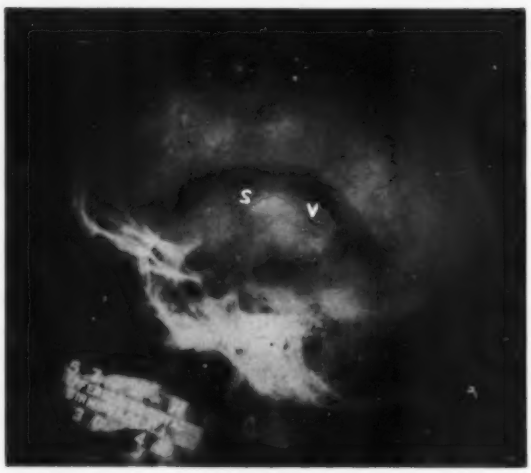

FIG. 7. Lateral view of skull with right side up, taken forty-eight hours following trephining. The air in the ventricles is less than in the still distinctly visible comma-shaped shadow caused by the coalescence of the cyst of the cavum pellucidum and the cyst of Verga. *S*, cyst of septum pellucidum; *V*, cyst of Verga.

faulty communication and also thickened walls of the cysts.

Following this procedure, the patient felt better for several weeks. However, the headache and convulsions returned later in an unabated manner. In view of the fact that the roentgenograms did not give any evidence for blocking of the cerebrospinal pathway, and also on account of the many psychoneurotic features of the case, no surgical attempt was made to correct the existing anomalies.

SUMMARY

The cyst of the cavum of the septum pellucidum and the cyst of Verga are not uncommon developmental anomalies which may occasionally give rise to clinical signs. They are divided into two groups, the communicating and the closed type, the latter being subdivided into the primary and acquired varieties. The closed group is more prone to cause mental and neurological syndromes. A correct diagnosis can be made only with air studies. In the open type, the usually co-existing fifth and sixth ventricles communicate with each other and appear as one long, comma-shaped shadow on the lateral view. The closed type of the cyst of the cavum of the septum pellucidum causes separation and bulging of the leaves of the septum pellucidum toward the lumen of the anterior horns while the closed cyst of Verga produces signs of displacement, often associated with production of internal hydrocephalus. A twenty-four hour, forty-eight hour or even later roentgenogram after the introduction of air into the ventricles should be taken because normally closed types of these cysts may be reopened during the alteration of the intracranial pressure following the drainage of the cerebrospinal fluid. Retention of air in these cysts is suggestive of a ball valve-like mechanism governing the communicating system between these cysts and the regular ventricular system. A fairly typical case is shown and the roentgenographic differential diagnosis is discussed.

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BENIGN GIANT CELL TUMOR OF THE SPINE

REPORT OF A CASE OCCURRING IN THE CERVICAL SPINE

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and
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THE occurrence of giant cell tumor of the cervical spine is thought to be sufficiently rare to justify reporting a case of benign giant cell tumor in which there was destruction of a part of the body, the laminae and the spinous process of the fourth cervical vertebra and in which there was complete recalcification of the tumor and relief of symptoms following roentgen therapy.

Rix and Geschickter,[29] in an analysis of 291 tumors of the spine, found 58 cases of primary tumors of which 15 were giant cell tumors. Kolodny,[17] in the analysis of the material of the Bone Registry in 1927, found that giant cell tumors occurred in the spine in 8 per cent of cases. In Table 1 are listed the cases that have been collected from the literature. Some cases may have been missed but the list is sufficiently complete to indicate that the cervical spine is an infrequent location of giant cell tumor of the spine, 12 out of 91 cases, or 13.1 per cent.

Several other reports are listed in the references but it is felt that these cases are included in those given in the table as they are either earlier reports by the same group of authors or from the same institution. Murphy's[25] case is interesting because he reports a giant cell tumor of the lumbar vertebra in which operation was thought inadvisable and in which the patient refused radiation therapy. The case was followed and healed by calcification. A pathological fracture had occurred and this probably stimulated healing.

While there is still disagreement regarding some phases of the pathology of giant cell tumor, it is now generally agreed that while a majority of giant cell tumors are benign, there are cases which are either malignant from the outset or which undergo malignant changes. Some pathologists prefer to use the term benign and malignant giant cell tumor to designate the two groups. For detailed discussion of the pathological features of the disease, the reader is referred to the publications by Rix and Geschickter,[29] Geschickter and Copeland,[11] and Jaffe, Lichtenstein and Portis,[14] Coley and Higinbotham[5] have briefly summarized the theories as to the

TABLE I

REPORTED CASES OF GIANT CELL TUMOR OF THE SPINE

Author	Year	Cases Giant Cell Tumor of Spine	Cases in Cervical Spine
Lewis[18]	1924	17	1
Kolodny[17]	1928	8	?
Cotton[6]	1928	1	0
Bower, Clark and Davis[1]	1930	14	1
Santos[30]	1930	2	1
Lindsay and Crosby[19]	1933	1	1
MacFarlane and Linell[20]	1933	1	1
Milch[24]	1934	1	1
Murphy[25]	1935	1	0
Peirce and Lampe[26]	1936	5	0
Duncan and Ferguson[8]	1936	1	0
Cleveland[7]	1937	1	1
Cabot Case 23081[4]	1937	1	1
Rix and Geschickter[29]	1938	15	1
Brunschwig[3]	1938	1	0
Jenkinson, Hunter and Roberts[15]	1938	2	0
Willard and Nicholson[35]	1938	1	1
Coley and Higinbotham[5]	1938	3	0
Richards and Singleton[28]	1938	2	1
Meyerding[21]	1941	10	1
Gershon-Cohen[12]	1943	3	0
TOTAL		91	12

mode of production or the cause of giant cell tumor as follows:

1. Neoplastic theory which assumes a true tumor originating in the bone marrow.

2. A non-neoplastic theory which holds that the condition is not a tumor but the result of chronic inflammation or chronic irritation, i.e. a faulty repair phenomenon.

3. Traumatic theory which assumes that an injury induces a subcortical hemorrhage in cancellous bone, and the area gradually extends and progressively destroys more and more bone.

Geschickter and Copeland[11] believe that the benign giant cell tumor is a phase of normal bone development which has extended beyond normal due to overactivity of the osteoclasts. Jaffe, Lichtenstein and Portis[14] would exclude the various variants of giant cell tumor. They disagree with many of the ideas advanced by Geschickter and Copeland.

While giant cell tumor can occur at any age, it is generally agreed that it most frequently occurs during the second and the first part of the third decade of life. Jaffe, Lichtenstein and Portis believe that if the various variants of giant cell tumor are excluded, the lesion will almost always be found in persons over twenty years of age, and that a considerable number of the tumors will prove to be malignant.

The spindle cell variants of the tumor occur commonly in vertebrae, flat bones, and bones of the hands and feet. They tend to heal readily and the prognosis is good. The case to be reported is a spindle cell variant type of giant cell tumor.

As pointed out by Kirklin and Moore,[16] roentgenograms of giant cell tumors may show the trabeculated appearance often described as the typical roentgen finding in giant cell tumor or may show a preponderantly lytic lesion with large areas of the bone completely absorbed. In the more advanced cases, the lytic areas may extend to the cortex, obliterating its shadow on the roentgenogram and the tumor may extend into the adjacent soft tissue. These authors suggest that the two types of roentgen findings probably represent different phases of the same process and not two different types of pathological change. The case to be reported is of the lytic type.

Roentgen therapy has long been recognized as a suitable means of treating benign giant cell tumor and its use has grown in favor with surgeons and pathologists as well as radiologists during the past twenty years. Kolodny[17] and many others advocate the use of radiation therapy without a biopsy in cases showing characteristic roentgen findings as recorded on the roentgenogram, and state that in those cases in which doubt exists as to the diagnosis from the roentgenogram the doubt will probably exist after study of the tissue. In their series, 20 per cent of cases treated by curettage recurred. In the group reported by Rix and Geschickter,[29] there was 25 per cent recurrence following curettement. Kolodny and others believe that when curettement is done and the lesion does recur, subsequent irradiation does not give as good results as in the uncuretted lesion. Another reason given for avoiding biopsy or curettage is the possibility of a superimposed infection following operation.

Brailsford,[2] in his excellent summary, states that the characteristic appearance of a giant cell tumor on the roentgenogram can be easily recognized. Because of the ease of diagnosis by one sufficiently experienced, and the excellent results from roentgen therapy it is unnecessary to do a biopsy. He gives the following limitations and disadvantages in regard to biopsy:

1. It does not reveal any additional features; it merely confirms the radiographic evidence; it may be misleading.

2. It weakens the stability of the bone; it may fracture the bone, or damage the joint surface, and make amputation appear essential.

3. It removes the scaffolding on which repair can be built up and so delays restitution.

4. It fails to reveal whether or not the tumor will form metastases. Tumors presenting the same histological structure may be eradi-

cated by local curetting or may metastasize and kill the patient.

5. It may actually disseminate the tumor cells.

6. It is an added risk to the patient.

7. There is evidence which suggests that the surgical trauma may incite malignant metaplasia in some cases.

Rix and Geschickter,[29] on the other hand, advocate curettement followed by roentgen therapy. Many surgeons advocate curettement and filling the defect with bone chips when the lesion is accessible, and give as one of the principal reasons for selecting this mode of treatment the fact that quicker end-results may be obtained. Where the lesion is located in the spine, the case is usually referred for roentgen therapy because of inaccessibility for surgery. It would seem that the mode of treatment will have to be determined at present for each case and that all phases of the individual case will have to be considered.

The dose of roentgen radiation most advocated has been a tumor dose of 3 to 5 erythemas delivered to the tumor over a period of several months in divided series, approximately 1 erythema dose at each series of treatments and the series of treatments administered at monthly intervals. One reason for the divided doses has apparently been that in some cases the tumor enlarges and symptoms are aggravated following roentgen therapy. After a few weeks the symptoms subside and the tumor undergoes recalcification. In the present case, the treatments were given at a little more rapid rate; there was no increase in the size of the tumor, and the patient experienced no aggravation of symptoms. Whether or not aggravation of symptoms is less apt to occur in the spindle cell variant of giant cell tumor cannot be determined from a review of the literature.

CASE REPORT

The patient was a male, aged twenty, who gave a history of having injured his neck and back in a truck accident September 1, 1942. There was considerable pain in the neck at this time and stiffness and some pain continued for a three month period. Early in 1943 he was accidentally struck in the neck and complained of stiffness and pain in the neck radiating down the right shoulder with weakness in the arm and numbness along the little finger. During this same period, there was a small amount of pain in the left arm and some numbness in the little finger of the left hand. The radiating pain and numbness became worse during April, 1943, and continued to slowly increase in intensity until August 14, 1943, when he entered an overseas station hospital. At that time a neurological examination did not reveal any evidence of organic pathology. Roentgenograms of the cervical spine made at that time showed a destructive lesion of the spinous process of the fourth cervical vertebra. Jarring of his neck caused sensory changes in the upper extremity and the patient complained of an increased amount of radiating pain down both arms and considerable weakness of both arms.

The patient was transferred to a general hospital overseas where a careful examination revealed that there was no muscle group atrophy or demonstrable weakness. A biopsy was done and a tumor which was grayish in color, moderately bloody, and quite friable, was found between the third and fifth spinous processes in the cervical area, apparently originating in the spinous process of the fourth cervical vertebra.

Roentgenograms made at the general hospital overseas revealed that the spinous process, the laminae, the inferior facets and portions of the superior facets of the fourth cervical vertebra showed complete loss of normal bone structure. The destruction was more marked on the right side than on the left. The bone that remained in the involved areas appeared to be finely honeycombed and of an amorphous character. The vertebral body of the fourth cervical vertebra appeared to be partly decalcified, but its main outline still appeared to be intact. The vertebrae above and below the fourth cervical showed no such destructive process, but there was a slight forward displacement of the body of the third on the fourth cervical vertebra as a result of the destructive lesion in the fourth cervical vertebra.

At the time the biopsy was taken, August 27, 1943, the blood sedimentation rate was 10 mm. per hour, phosphoesterase 1.5 Bodansky units,

serum calcium 10.8, phosphorus 4, blood count normal, serology negative, urine normal, spinal fluid count cell count 2, gold curve normal, spinal fluid protein 50 mg. per 100 cc.

The patient was admitted to Letterman General Hospital September 30, 1943. Roentgen

Fig. 1. November 4, 1943. Roentgenogram showing destruction of the spinous process, both laminae, and a portion of the body of the fourth cervical vertebra.

examination of the cervical spine at this time confirmed the previous findings and showed a little more destruction of the vertebral body, but there were no other apparent changes. There had been no apparent change in the subjective symptoms which the patient suffered and his head had been supported in a cast or a traction apparatus since he first reported to the station hospital overseas. There was considerable pain in the neck and some radiating pain down both arms when the least amount of motion of the neck was allowed. The neurological examination was also negative. All of the laboratory procedures were repeated and the previous negative findings were confirmed. A complete skeletal survey did not reveal any other areas of involvement. The patient was presented to the tumor board and treatment was delayed until the diagnosis of the tissue removed at the biopsy could be confirmed by the pathologists at Letterman General Hospital and the opinion of the Army Medical Museum obtained. After all of the data had been assembled, roentgen therapy was started on November 3, 1943.

Report of Tissue From Overseas Hospital. Gross: Specimen consists of several small pieces of brownish-gray tissue, the largest of which measures 1.5 by 1.6 by 0.3 cm. Some of these specimens contain small spicules of bone. Cross section of the pieces that do not contain bone reveals a grayish-brown surface in which a few flecks of hemorrhage are seen. The outer surfaces of the specimens are almost warty in character. Cross section reveals a few hemorrhagic areas in the tissue. The tissue is very friable. Microscopic: Section consists of neoplastic tissue in which several features of interest are noted. The stroma is composed of two types of cells. The great majority are connective tissue spindle cells showing no hyperchromatism and exhibiting no mitoses. The other cell type present is the endothelial cell. It is thought that these are the origin of the giant cells. Xanthoma cells are seen. These are

Fig. 2. December 17, 1943. Roentgenogram made six weeks after the administration of 1,380 r to the tumor shows considerable recalcification of the entire tumor area.

pale, epithelioid and probably contain fat or cholesterol esters. A moderate amount of hemosiderin pigment is scattered diffusely through the section. Numerous small capillaries

FIG. 3. February 6, 1944. Roentgenogram showing further recalcification, one month after completion of second course of roentgen therapy. The second series consisted of 690 r delivered to the tumor.

are found and one or two areas of hemorrhage are seen. There is evidence of bone necrosis, for two areas in the section are bluish staining, amorphous and resemble necrotic bone tissue. No osteoblasts are seen and no osteogenic activity is noted. The unusual feature of the section is the presence of a moderate number of giant cells. These contain from 5 to 35 small, separate nuclei. They are not hyperchromatic. The cytoplasm is granular and pink-purplish staining. These nuclei pack the cell and some are clumped in the center. None are peripherally arranged. No capsule is seen in these sections. A moderate amount of collagen is present in the stromal tissue.

This tissue falls into the benign giant cell tumor group. There is no evidence of osteogenic sarcoma, carcinoma or tuberculosis. Because of the difficulty of completely removing all of the tumor tissue and mindful of the fact that repeated curettage occasionally transforms these tumors into malignant growths, roentgen therapy is probably the treatment of choice in this case. Diagnosis: Giant cell tumor of bone, benign.

Microscopic Examination at Letterman General Hospital. In areas, the lesion presents the typical appearance of benign giant cell tumor. Other portions of the growth, however, are more fibroblastic and show associated production of cartilage and osteoid tissue. It is not entirely clear whether these latter areas are compatible with a healing process in a malignant lesion. It is considered possible that we may be dealing with a secondary giant cell reaction in a malignant bone tumor. One fragment of the specimen consists of acute inflammatory exudate. The material is being forwarded to the Army Medical Museum for consultation.

Army Medical Museum Report. The diagnosis in this case is believed to be the so-called

FIG. 4. April 1, 1944. Final roentgenogram showing complete recalcification of the entire tumor. The total amount of roentgen radiation delivered to the tumor was 2,070 r and was concluded three months before this roentgenogram was taken.

fibrous dysplasia of bone. It will be noted that the main lesion is a fibrous one from which metaplastic bone trabeculae are formed. The occasional giant cells present appear to be osteoclasts in the region of hemorrhage, both fresh and old. The presence of cartilage in this lesion is not contradictory. It would be interesting to know whether there are multiple lesions in this case.

In spite of the slight disagreement in the microscopical diagnosis, it was felt that when all of the findings in the case were considered, we were dealing with a giant cell tumor and that roentgen therapy was the treatment of choice.

Therapy. Between November 3 and 13, 1943, the patient received 1,000 r roentgen radiation to each of two lateral 10 by 10 cm. fields centered over the involved area. Alternate fields were used daily. The factors used were 200 kv.; added filtration 0.5 mm. Cu plus 1.0 mm. Al; 18 ma.; output 28.5 r per minute, measured in air; 50 cm. skin target distance; half-value layer, 0.9 mm. Cu. The estimated dose delivered to the center of the tumor was 1,380 r.

Between January 1 and 5, 1944, 500 r additional was given to each field, treating both fields daily. The factors used were the same and the estimated tumor dose for the second series of treatments was 690 r, which made the total tumor dose for the two series of treatments 2,070 r.

Roentgenograms of the cervical spine made on December 17, 1943, showed extensive recalcification of the tumor, the main portion of the mass lying in the space between the spinous processes of the third and fifth cervical vertebrae. At an earlier date, the patient had noticed that the pain in his upper extremities on the slightest motion of the head had diminished and by December 17, 1944, this pain had practically disappeared. During all this time, and until the middle of March, 1944, the head and neck were supported either by a body cast or a special brace. The fact that this support was constantly applied from the time the lesion was first discovered until complete recalcification occurred is probably responsible for the fact that the lesion healed without any deformity of the spine and with no damage to the spinal cord. Roentgenograms made at intervals of a few weeks after December 17, 1944, showed increasing density of the callus. By mid March, 1944, the callus appeared so firm that the brace which supported the head and neck was discarded. There was no recurrence of the pain which had completely disappeared before this time. Neurological examination was again negative and the patient was judged to be apparently cured and transferred to another Army hospital for observation and disposition.

SUMMARY

The incidence of giant cell tumor of the spine is briefly reviewed, and the incidence of involvement of the cervical spine noted.

A case is reported which was diagnosed as a spindle cell variant of giant cell tumor on the basis of the history, physical and roentgen findings and study of tissue removed at biopsy, although there was some disagreement as to the microscopical interpretation of the tissue. Complete recalcification occurred following roentgen therapy with relief of the patient's symptoms. It is believed that the good result obtained (healing without deformity of the spine) was influenced by the fact that adequate support was applied to the head and neck from the time the lesion was first discovered and to the fact that no extensive curettage was done.

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HYPERTROPHIC OSTEOARTHROPATHY

CASE REPORT*

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IN 1935 a patient was admitted to the Medical Service of the University Hospital, Ann Arbor, Michigan, with pronounced clubbing of the fingers and toes associated with widespread skeletal involvement. Interest in the general subject of hypertrophic osteoarthropathy was thus provoked and a brief review was published in the *University Hospital Bulletin*[4] but without any illustrations from this interesting case. During this interval nothing has come to my attention that so well illustrates the universal distribution occasionally seen in this syndrome and for this reason the opportunity has been taken to report the case in some detail.

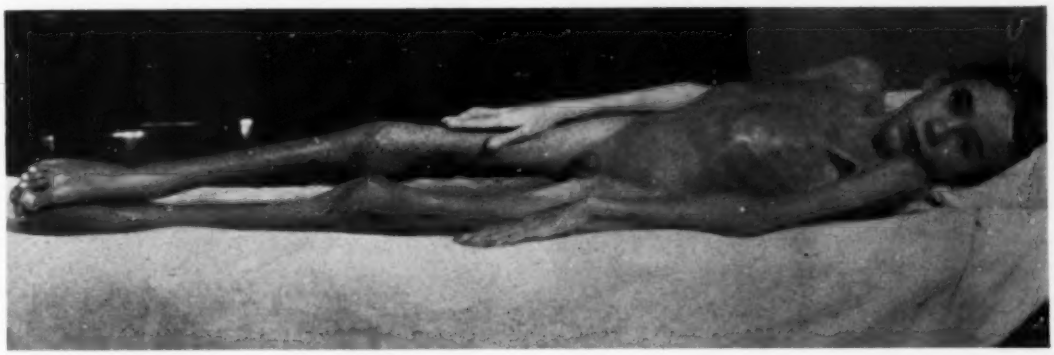

FIG. 1. Extreme emaciation, genital underdevelopment, lack of pubic hair, and marked clubbing of the fingers and toes.

CASE REPORT

W. K., male, white, aged fourteen, was admitted to the University Hospital November 7, 1935. The present illness dated back to 1925 when the patient was four years old. At that time he had a painless swelling of the right knee from which tuberculous material was removed at operation. The next year his mother noticed a lump on his back and he was admitted to another hospital with a diagnosis of Pott's disease involving the fifth, sixth and seventh dorsal vertebrae. This gradually subsided and from the age of eight to thirteen he was well enough to attend school. Numerous roentgenographic studies were made of the skeleton and the chest but at no time was there evidence of pulmonary involvement.

One year before admission, pulmonary symptoms commenced. At first there was only slight cough but five months before entry the cough became much worse and was accompanied by marked shortness of breath. There were occasional chilly sensations, night sweats, and great loss of weight.

Physical Examination. The temperature was 102.2° F., pulse 140, respirations 36, and blood pressure 120/50. The patient was an extremely emaciated and malformed boy whose development was about that of a ten year old child (Fig. 1). The skin was dry and bronzed in color. The eyes were deep set, the pupils being normal and reacting to light and in accommodation. There was a fetid odor to the breath, but the teeth were in fairly good condition. Examination of the thorax showed a tremendous flare of the costal margins with prominent ribs and

* I wish to express my appreciation to the Departments of Medicine and of Roentgenology of the University of Michigan for permission to publish the case and to Dr. John F. Holt and Dr. Harry Hauser for help in collection of material and preparation of the manuscript.

Fig. 2. Marked clubbing of fingers and toes.

Fig. 3. Roentgenogram of the chest showing the large abscess cavity in the left apex and the paravertebral abscess extending beyond the right hilum.

thin chest wall. The percussion note was hyperresonant except at the left apex where there was dullness. In this same area there was marked harshness of the breath sounds and many crackling râles. The heart was overactive and a systolic murmur was audible over the entire precordium. There was an operative scar in the left flank. No abdominal viscera were palpable. Superficial lymph nodes were enlarged. There was no pubic or axillary hair and the genitals were underdeveloped. The extremities were thin with marked clubbing of the fingers and toes (Fig. 2).

Laboratory Studies. An anemia with 58 per cent hemoglobin and 2.72 million erythrocytes per cubic millimeter of blood was present. The

Fig. 4. The paravertebral abscess in the dorsal region is better demonstrated in this view. Numerous calcified tuberculous foci are present in the spleen. Vertebral destruction is seen in the regions of the sixth to the ninth thoracic, first and second lumbar and first sacral segments.

cells were slightly hypochromic. The white blood cell count was 12,500 per cubic millimeter of which 76 per cent were polymorphonuclear cells. A glucose tolerance test was normal; the blood phosphorus was 3.9 mg. per 100 cc. and the calcium 8.9 mg. per 100 cc.

Ten direct examinations of the sputum for tubercle bacilli were negative although these organisms were cultured from both the sputum and gastric washings.

Roentgen Studies. A posteroanterior roentgenogram of the chest (Fig. 3) showed a large cavity with a fluid level occupying the left apex and a less well defined semicircular shadow of increased density extending out from the right hilum. This shadow on the right was demonstrated to contain fluid when heavy exposures with a Potter-Bucky diaphragm were made (not illustrated).

Fig. 5. Lateral view of the spine better demonstrating the destruction of the vertebral bodies.

A single anteroposterior roentgenogram of the thorax and abdomen (Fig. 4) showed destruction of the vertebral bodies in the regions of the sixth, seventh, eighth and ninth thoracic, first and second lumbar and first sacral segments. Numerous calcified nodules were seen in the region of the spleen. The crescentic shadow in the right hilum was again shown and was considered to represent a paravertebral abscess.

There was a symmetrical and almost universal elevation of the periosteum with subperiosteal new bone formation. This was most striking in the long bones (Fig. 6, 7, 8, 9 and 10) where it extended from the proximal to the distal epiphysis, but was also present to a less pronounced degree in the left scapula, clavicles, and ribs (Fig. 3 and 4). This lamination gave an "onion skin" appearance and at the distal end of the left humerus five distinct layers could be seen (Fig. 7 and 8*B*). Generalized osteoporosis was present.

Clinical Course. The patient was given

Fig. 6. Anteroposterior views of tibiae demonstrating periosteal new bone formation extending from the proximal to the distal epiphysis. Osteoporosis is pronounced.

transfusions and general supportive treatment. The spine was fixed by a posterior plaster shell and anterior frame. The pulmonary disease was so far advanced that no specific measures could be employed. He was transferred to another hospital for sanatorium care where he died March 7, 1936. No autopsy was performed.

The soft tissue manifestations of clubbing have attracted the attention of clinicians since the time of Hippocrates (whence the term hippocratic finger).[3] It was not un-

til 1889 when von Bamberger[1] reported 2 cases of bronchiectasis with skeletal involvement that correlation of clinical and pathologic findings was begun. Pierre Marie[5] reported the same condition one year later and attached to it the name of hypertrophic pulmonary osteoarthropathy. Although von Bamberger had priority, the condition is usually known by the name with which Marie designated it, less frequently as Marie's disease or Marie-Bamberger disease. Now that it is known that the bone changes may be secondary to other than pulmonary lesions this part of the name has been dropped and the condition is known simply as hypertrophic osteoarthropathy.

Fig. 7. Subperiosteal new bone formation involving the upper extremities.

Fig. 8. Better demonstration of the laminated character of periosteal new bone formation of (*A*) left tibia and fibula and (*B*) left humerus. Magnification ×1.5.

Fig. 9. Periosteal calcification less pronounced in femora.

Many theories have been advanced to explain the pathogenesis of this interesting condition. In general, most cases have seemed best explained either by "the toxic theory" or the "defective circulation theory."

Von Bamberger[1] and Marie[5] believed that the condition resulted from a toxin liberated by the bacterial decomposition of the bronchial secretions. Working on this hypothesis von Bamberger was the first to

attempt to produce the condition experimentally. He injected the bronchiectatic secretions into the rectum of young rabbits but his results were negative. Compere, Adams and Compere[2] were unsuccessful following artificially induced pulmonary collapse and lung abscess in dogs. More recently attention has been directed toward the circulation as the underlying defect. Mendlowitz and Leslie[7] simulated con-

Fig. 10. The bones of the right hand show definite hypertrophic periosteal changes in the shafts of the metacarpals and proximal phalanges. There is marked osteoporosis.

gential heart disease in dogs by anastomosing the left pulmonary artery to the left auricle. In one of two animals which showed increased cardiac output following this procedure, a definite subperiosteal proliferation developed which was similar grossly and histopathologically to hypertrophic osteoarthropathy. Mendlowitz[6] has published recently a communication on "Clubbing and Hypertrophic Osteoarthropathy" which is complete in all details and includes an excellent review of the literature to date.

The case reported here illustrates in a typical way the general features of the condition when it is present to an advanced degree. The long bones are nearly all involved, the distal epiphyseal region being more affected than the proximal as in the case of the humeri, tibiae, and fibulae. The profound osteoporosis characteristically accompanies the advancing periostitis either as an integral part of the process or as a result of the general debilitation of this individual. The distinctiveness of the laminations is remarkable and suggests that the factors operating in its production were not continuous but rather that these layers represent mile posts marking separate stages in the long illness of this patient.

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Twenty-eighth Annual Meeting: 1945, canceled.

EDITORIAL

BONE CHANGES IN ELECTRIC CURRENT INJURIES

THE increase in the use of electric current, not only the high tension current which supplies the city lighting systems and the great manufacturing industries, but the lower voltage household current which runs the various modern gadgets to lighten the many household duties, brings with it an increase in the number of injuries resulting from electric current accidents and burns.

The literature dealing with injuries due to electric current is not an extensive one. However, Palugyay as early as 1924 called attention to certain bone changes occurring in electric burns and he presented in a discussion of two cases the roentgen picture in bone injuries, particularly those of the upper extremities, namely the hands. Very little information has been added to this early description of these bone changes, which would seem to indicate that this is a chapter somewhat neglected in roentgen studies.

The most common bone change accompanying electric burns or injuries is the bone atrophy of the particular extremity involved in the accident and accompanying this bone atrophy is a sclerosis or hypertrophy of the periosteum, sometimes with alterations in the contour of the bone structure and rarefactions in the shaft of the bone, and occasionally a clear cut demarcation with sequestra formation.

The bone atrophy presents itself as a typical picture in the marked lessening of the calcium content (halisteresis), and this extensive loss of calcium content may involve all the bones of the injured extremity. This extreme atrophy may present itself as a roentgen picture several days after the injury, and indeed this is the usual occurrence. Associated with this loss of calcium content there may be a so-called cylindric sclerosis of the periostem, which type of sclerosis not only occurs in the diaphyses involved in the initial injury, but also the neighboring diaphyses, and this sclerosis may involve the bone structure even though the initial injury does not occur in the soft tissues immediately adjacent. The periosteal sclerosis may be a rather late manifestation, that is a matter of days following the shock or burn. The sclerosis is similar to that observed in spina ventosa or in an osteomyelitic process. This sclerosis when first observed may conform rather closely to the shaft of the bony contour; later the sclerosis appears to be separated somewhat from the bone by a translucent zone as if the periosteal proliferation is elevated from the shaft of the bone, and consequently there may appear along the shaft of the bone a rather thick calcium deposit.

Palugyay was not certain whether this so-called periosteal sclerosis represents an inflammatory reaction or results from a direct injury to the cells of the periosteum bringing about an ossification, or whether the changes are due to a subperiosteal hemorrhage.

Jaffé believes it is probable that the extensive bone changes are due not only to the initial electrical shock and the burn itself, but also to the changes brought about in the blood vessels and the nerves.

It is the extreme atrophy of the bone structures of the injured extremities which is the striking roentgen finding, and the periosteal reaction may not be observed. Associated with these marked bone changes is a certain degree of fuzziness or indistinctness in the appearance of the contour of the bones, and there is not infrequently a softening of the bone structures leading to contractural deformities of the extremity,

with considerable thickness of the cortex toward the end of the process, and not infrequently there may be actual sequestration of the necrotic bone. The type of atrophy which involves the skeleton is somewhat similar to that observed in Sudeck's atrophy.

In the initial bone changes, there may appear fine and delicate lines as shown in the roentgenogram. On superficial observation these are quite difficult to distinguish from normal bone structure and curiously enough these lines may not appear for two or three weeks and they present themselves in linear, zigzag or stellate type of bone pattern. These are among the earliest manifestations of the effect of electrical burns in the living bone, the extensive osteoporosis appearing sometimes weeks later, and associated with this osteoporosis there may be spontaneous fractures with sequestra as described. Unless the roentgenograms are examined carefully in cases suffering from electrical burns these earliest manifestations may be completely overlooked.

It is with the bone changes in electric current injuries that the roentgenologist is primarily concerned. Since Palugyay's communication describing these changes little of interest or importance has been added even by the later observers, and there are implications in this fact that further observations and experimental work on the skeletal changes in electric current injuries are needed.

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Jaffé, R. H. Electropathology; review of pathologic changes produced by electric currents. *Arch. Path.*, 1928, *5*, 837–870.

Jellinek, S. Changes in electrically injured bones. *Brit. J. Radiol.*, 1926, *31*, 23–25.

Pearl, F. L. Electric shock; presentation of cases and review of the literature. *Arch. Surg.*, 1933, *27*, 227–249.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: 1945, canceled.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago.

Section on Radiology, American Medical Association
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio. Annual meeting: 1945, canceled.

Arkansas Radiological Society
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1945, to be announced.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Section on Radiology, California Medical Association
Secretary, Dr. Gordon G. King, 3700 California St., San Francisco 18, Calif.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles County Medical Association
Secretary, Dr. Roy W. Johnson, 1407 S. Hope St., Los Angeles, Calif. Meets on second Wednesday of each month at the County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

Chicago Roentgen Society
Secretary, Dr. F. H. Squire, 1754 W. Congress St., Chicago 12, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meetings held in Dallas on odd months and in Fort Worth on even months, on third Monday, at 7:30 P.M.

Denver Radiological Club
Secretary, Dr. A. Page Jackson, Jr., 1612 Tremont Place, Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida Radiological Society
Secretary, Dr. J. F. Pitman, Blanch Hotel Annex, Lake City, Fla. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meets annually second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Michigan Association of Roentgenologists
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

New Hampshire Roentgen Ray Society
Secretary, Dr. Richard C. Batt, Berlin, N. H. Four meetings a year.

Radiological Society of New Jersey
Secretary, Dr. H. R. Brindle, 501 Grand Ave., Asbury Pk. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. An-

*** Secretaries of Societies not here listed are requested to send the necessary information to the Editor.**

nual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Henry Snow, 1061 Reibold Bldg., Dayton, Ohio. Meets during annual meeting of Ohio State Medical Association.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. C. L. Stewart, Jefferson Hospital, Meetings first Thursday of each month, October to May, at at 8:00 P.M., in Thomson Hall, College of Physicians, 21 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. L. M. J. Freedman, 4800 Friendship Ave. Meets 6:30 P.M. at The Ruskin on second Wednesday, each month, October to May inclusive.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary Dr. A.M. Popma, 220 N. First St., Boise, Idaho.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

SAN DIEGO ROENTGEN SOCIETY
Secretary, Dr. Henry L. Jaffe, Naval Hospital, Balboa Park, San Diego, Calif. Meets monthly on first Wednesday at dinner.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. Carlton L. Ould, University of California Hospital, San Francisco 22. Meets monthly on the third Thursday at 7:45 P.M., first six months of the year at Lane Hall, Stanford University Hospital, and second six months at Toland Hall, University of California Hospital.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, Monday, January 14, 1946.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October through May, College Club, Seattle.

X-RAY STUDY CLUB OF SAN FRANCISCO
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly, third Thursday evening.

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY
Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets on the third Friday of each month at 4:45 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

FACULTY OF RADIOLOGISTS
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

SECTION OF RADIOLOGY AND MEDICAL ELECTRICITY, AUSTRALASIAN MEDICAL CONGRESS
Secretary, Dr H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Secretary, Dr. J. W. McKay, 1620 Cedar Ave., Montreal, P. Q.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL ASSOCIATION
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

SOUTH AMERICA

SOCIEDAD ARGENTINA DE RADIOLOGIA
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

SOCIEDAD PERUANA DE RADIOLOGIA
Secretary, Dr. Victor Giannoni, Apartado, 2306, Lima, Peru. Meetings held monthly except during January, February and March, at the Asociación Médica Peruana "Daniel A. Carrión, Villalta 218, Lima.

CONTINENTAL EUROPE

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SOCIÉTÉ SUISSE DE RADIOLOGIE (SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT)
Secretary for French language, Dr. Babaiantz, Geneva.
Secretary for German language, Dr. Max Hopf, Effingerstrasse 49, Bern. Meets annually in different cities.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

MOSCOW ROENTGEN RAY SOCIETY
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

LAURISTON S. TAYLOR HONORED

The Bronze Star Medal for meritorious service was presented on October 26, 1945, to Dr. Lauriston S. Taylor, 4923 Battery Lane, Bethesda, Maryland, by Major General Samuel E. Anderson, Chief of Staff, Continental Air Forces, in General Anderson's office at Bolling Field, D. C. Dr. Taylor, who has been associated with the Operations Analysis Branch of the Army Air Forces, served in the European theater of operations from May, 1943, until June, 1945, being stationed in England, France, Belgium, Germany and Luxemburg.

The citation accompanying Dr. Taylor's award commended him for outstanding leadership, analytical ability and technical skill demonstrated while he was chief of the Operational Research Section of the 9th Bombardment Division. Under his direction, the efficiency of lead crews increased, a highly efficient program of bridge interdiction was scheduled and bombing accuracy greatly improved.

Dr. Taylor arrived in France shortly after D-Day to aid in an investigation of enemy targets hit by allied aircraft for an assessment of the effectiveness of our weapons against these targets.

A graduate of Cornell University, Dr. Taylor is a member of the American Physical Society, the Washington Academy of Medicine, the American Roentgen Ray Society and the Radiological Society of North America. He plans to return to his pre-war position as Chief of the X-Ray Section, Bureau of Standards, in Washington, D. C.

BRITISH HOSPITAL PHYSICISTS ASSOCIATION DIAGRAMS AND DATA SUB-COMMITTEE

Charts and diagrams often appear in the radiological literature which are too small to be of practical use; it would be convenient if there were some way of obtaining full size copies of the originals. Also institutions accumulate diagrams and data for their own use, which are not published but which would be useful to others if they were available.

The British Hospital Physicists Association has undertaken to provide such a clearing-house, and has issued a catalog of some 200 items which are available. These comprise a wide range of isodose curves and dosage calculation charts for roentgen rays and radium, diagrams of apparatus, tables of mathematical data, and a few books. Anyone having data to share can list it with the Secretary of the Association and anyone wishing to obtain any of the items can order them through him. The cost per item is moderate, and it is expected that it will be reduced when the scheme has been in operation long enough to build up a small reserve.

Detailed information as to what data are available, and current charges therefor can be obtained from the Secretary, Dr. J. Read, Radiotherapy Department, The London Hospital, Whitechapel Road, London E 1.

This is an excellent idea and one that might well be copied by radiological physicists in this country. Cooperation could then be developed between British and American groups for their mutual profit. No American organization exists analogous to the British Hospital Physicists Association, but physicists are well represented on the Standardization Committees of both the American Roentgen Ray Society and the Radiological Society of North America, and such a plan might come within their scope. Or it might appropriately be an activity of the American College of Radiology, with an advisory committee of physicists and radiotherapists. It is suggested that the subject be put before the various interested groups for consideration.

"COMMITTEE ON GROWTH" OF THE NATIONAL RESEARCH COUNCIL

The appointment of a Committee on Growth, with membership designed to be

broadly representative of the fields concerned in cancer research, both basic and clinical, has already been announced by the National Research Council of the National Academy of Sciences. The Committee was created, within the Division of Medical Sciences of the Council, as a result of action by the American Cancer Society designating the Academy as its scientific adviser for research.

The Committee wishes to call the attention of interested investigators to the general outline of endeavor which it proposes to foster and the general principles by which it will be guided. The Committee accepts the interpretation of its field of interest as including reliance on, contact with and support of research in the basic sciences bearing broadly on the whole phenomenon of growth.

The Committee has adopted the following major principles by which, so far as possible, it will be guided in its sponsorship of research and training programs:

(a) Desirability of long-term grants to projects of major importance.
(b) Grants, where possible, of such magnitude as to permit individual investigators to appoint associates for long-term training periods.
(c) Granting of fellowships to institutions for training of workers to acquire new techniques and wider experience.
(d) Maintenance of continuing individual contact with workers in the field.
(e) Provision, on a participating basis, for continuing economic security for professional workers.
(f) Liberal attitude toward the investigator's work, his publication and reports.

To assist it in the fulfillment of its advisory functions the Committee, on its part, will make free use of either *ad hoc* or standing subcommittees in specific fields of interest. Furthermore, it proposes to arrange conferences of competent groups for discussion of problems, for interchange of reports, etc.; make surveys to analyze problems or to determine progress in areas of special interest pertaining to cancer; evaluate, through study by subcommittees and by the main committee, basic and clinical research undertakings, and submit recommendations for support to the American Cancer Society; initiate and plan broad or specific programs of basic and clinical research, through activities of the subcommittees and main committee, and secure the cooperative efforts of investigators in the general undertakings.

The Committee has established a central office in the Washington headquarters of the Council where information on all phases of cancer research will be assembled and from which reports may be distributed to interested investigators.

Many members of the Committee have participated intensively in the broad programs of research conducted under the pressure of war. It is both the hope and the sanguine expectation of the Committee that the fruitful pattern of cooperative investigations so successfully established during the war years, can now be carried on, modified and tempered to existing needs, into the continuing war against disease.

Membership of the Committee, as now constituted, includes the following: Dr. C. P. Rhoads, *Chairman*, Dr. Florence R. Sabin, *Secretary*, Dr. A. R. Dochez, Dr. A. Baird Hastings, Dr. Charles B. Huggins, Dr. Donald F. Jones, Dr. C. C. Little, Dr. Carl R. Moore, Dr. John J. Morton, Dr. James B. Murphy, Dr. Eugene P. Pendergrass, Dr. Howard C. Taylor, Jr., Dr. M. A. Tuve, Dr. M. C. Winternitz.

Philip S. Owen, M.D. *For the Committee on Growth, Division of Medical Sciences, National Research Council.*

2101 Constitution Ave.,
Washington 25, D. C.

EXHIBIT ON BONE TUMORS

A committee of the American Roentgen Ray Society was appointed consisting of Dr. C. H. Heacock, Chairman, Dr. Ross

Golden and Dr. C. E. Hufford to confer with Colonel A. A. deLorimier regarding the disposition of the extensive Exhibit on Bone Tumors of the late Dr. John T. Murphy of Toledo. The following decision has been made:

1. The original exhibit will be maintained permanently in Washington, D. C., in the Army Medical Museum.

2. The Army School of Roentgenology will make two copies of the exhibit. One set will be retained by the School for use in teaching. The other set will be the property of the American Roentgen Ray Society.

CELEBRATION OF FIFTIETH ANNIVERSARY OF DISCOVERY OF THE ROENTGEN RAY

Various professional and lay groups interested in the roentgen ray are celebrating the Fiftieth Anniversay of its discovery at a meeting to be held in the Cleveland Medical Library, Cleveland, Ohio, on November 8, 1945. In the afternoon there will be talks by a representative of one of the universities, a radiologist, a dentist, and a research industrialist. In the evening, after a short historical program, there will be an exhibit illustrating the uses of the roentgen ray in medicine, dentistry, public health and industry. The exhibit will be open to the public on Sunday afternoon, November 11.

The committee consists of Dr. Howard Dittrick, Chairman, J. T. McCarthy, L. O. Olson, H. J. Wallace, Dr. J. S. Driver, Dr. Otto Glasser, Dr. Harry Hauser, and Dr. J. A. Sweeney.

NEW ENGLAND ROENTGEN RAY SOCIETY

At the meeting of the New England Roentgen Ray Society to be held on November 16, 1945, at eight o'clock at the Harvard Club, Boston, the Fiftieth Anniversary of the discovery of the roentgen ray will be commemorated by the following special program:

The Use of Roentgen Rays in Art. William J. Elliott, M.D., Worcester, Mass.

Some Industrial Applications of Roentgen Rays. Paul E. Tivnan, M.D., Beverly, Mass.

The Application of Roentgen Rays to Crime Detection. Joseph T. Walker, Ph.D., Chief of State Police Laboratories.

Roentgen Rays as a Tool of the Physicist. Bertram E. Warren, Sc.D., Cambridge, Mass.

Roentgen Rays in Medicine. Merrill C. Sosman, M.D., Boston, Mass.

SEGUNDO CONGRESO MEXICANO DE CANCER

A cordial invitation is extended to the members of the American Roentgen Ray Society to attend the Segundo Congreso Mexicano de Cancer and Tercera Semana Medica de Occidente to be held in Guadalajara, Mexico, February 3 to 9, 1946. The President is Dr. Manuel Ribeling and the Secretary is Dr. Enrique Garcia Ruiz, Edificio Lutecia No. 123, Guadalajara, Jal., Mexico.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

X-Ray Isodose Curves. Compiled by the Staff of the Physics Department of the Royal Cancer Hospital (Free), London, S.W. 3. 45 kv., 60 kv., 140 kv. (peak), 200 kv., 400 kv. (peak), isodose curves. Reprint of Percentage Depth Dose Tables supplied with each set of curves. Isodose curves contained in stout cardboard portfolios. Complete set at £10.10*s.*0*d.* Royal Cancer Hospital (Free), Fulham Road, London, S.W. 3, England.

Tables and charts readily available to American radiologists give roentgen-ray depth doses along the axis of the radiation beam, for almost any desired set of physical factors. For points off the axis the dose is known to be less than that in the central position; toward the edge of the field the difference becomes marked. For satisfactory determination of dosage at any position off the axis, isodose charts are essential. Scattered charts of this sort are to be found in the literature, as parts of articles on radiation measurement; few of these are convenient for regular use, even if they present desired factors.

The Physics Department of the Royal Cancer Hospital (Free), recognizing the need for a wide variety of charts of this sort, has prepared a set covering a considerable range of qualities and field sizes. These are based on experimental work at the Hospital, supplemented by data from the literature. Each chart is printed in black, red, or green, on fairly transparent tracing linen, in actual size, so that it is convenient for use with life-sized anatomical diagrams.

The complete set comprises 66 charts as follows:

45 kv.—6 charts, small fields and short distances, appropriate to Philips contact equipment. Cost, £1.11*s.*6*d.*

60 kv.—8 charts, small fields and short distances, appropriate to Chaoul contact equipment. Cost, £1.11*s.*6*d.*

140 kv. (peak), 0.25 mm. Cu filter, 0.32 mm. Cu half-value layer (approximately 7 mm. Al half-value layer), 9 charts, small and medium fields, 15–25 cm. distance. Cost, £2.2*s.*0*d.*

200 kv. (peak), 1.0 mm. Cu plus 1.0 mm. Al filter, 1.5 mm. Cu half-value layer, 22 charts, small, medium, and large fields, including long and short axis for a few rectangular fields, 50 and 80 cm. distance. Cost, £3.3*s.*0*d.*

400 kv. (peak), 0.22 mm. Sn plus 1.7 mm. Al filter, 3.6 mm. Cu half-value layer, 21 charts for essentially the same fields and distances as the 200 kv. group. Cost, £3.3*s.*0*d.*

The 45 and 60 kv. sets are applicable only to the Philips and Chaoul contact equipment respectively. It should be noted that the former are drawn twice actual size. It is the opinion of this reviewer that the 140 kv. (peak), 0.25 mm. Cu filter combination is not now widely employed in this country.

The values for the doses along the axis of the beam, for 200 and 400 kv. (peak) are in good agreement with data currently used in the United States; these charts should be useful to every radiologist for determination of dose to any part of a region under treatment. Qualities corresponding to half-value layers of 1.0 or 2.0 mm. Cu are probably more frequently employed here than 1.5 mm. Cu. However, since in this range differences are not large, satisfactory values for either 1.0 or 2.0 mm. Cu half-value layer can be obtained by making slight corrections. Values for distances and fields not included in the set can be determined by interpolation with the aid of tables.

The preparation of these charts has been painstaking, and radiologists are indebted to Dr. Mayneord and his associates for the manner in which it has been accomplished. It is to be hoped that they will be encouraged to provide others for the 100 kv. (peak) region, at 15 to 25 cm. distances, and for million volt beams.

Edith H. Quimby

Les bases physiques et biologiques de la roentgenthérapie. Par Paul Lamarque, Docteur ès Sciences; Professeur à la Faculté de Médecine de Montpellier; Directeur du Centre Régional contre le Cancer. Avec la collaboration de MM. Pierre Bétoulières, Jean Reboul, Edmond Debains et Pierre Lorimy. Préface de Mr. le Professeur Strohl. Paper. Pp. 530, with 284 illustrations. Paris: Masson et Cie, 1942.

Convinced that clinical radiology will make little further progress until radiologists are familiar with its basic physics and biology, the

author has undertaken to assemble this material in a comprehensive volume, and has done it well.

The nature and behavior of roentgen rays are thoroughly discussed, but with a minimum of mathematics. Roentgen-ray tubes of many types are described, and numerous transformer-rectifier circuits presented. The chapter on qualitative measurements is the best this reviewer has seen on that topic, including spectrometry, voltage measurements of various types, and the different schemes based on absorption measurements. Under quantitative measurements, a number of standard dosimeters are described in some detail. The section on practical dosimetry is rather disappointing in that it contains insufficient data for dosage calculation in actual therapy.

Basic radiobiology is as well handled as basic physics. Reversible and irreversible effects on the living cell, the phenomenon of radiosensitivity, and quality, intensity, and time factors are discussed. The action of roentgen rays on various tissues and organs is set forth in detail; relative radiosensitivities are given, and related to therapeutic possibilities, especially in the treatment of functional and inflammatory conditions. In relation to the biologic basis of clinical dosimetry, the importance of a study of tissue recovery is emphasized.

Radiation therapy techniques are discussed from the points of view of radiation quality, and of the spatial and temporal distribution of the dose. Under the first heading, much attention is given to very soft radiations—Bucky, Philips, and Chaoul type of equipment. Under the last, various techniques for fractionation of dose are presented, with little critical attention to discrepancies in the numerical data of different authors.

The hazards of radiation to patients and to personnel of a department of radiology are thoroughly discussed and desirable protective measures are outlined. The national French regulations are included.

A final chapter by Reboul contains an excellent summary of the various theories of biological action of radiation.

The book ends with an extensive bibliography, which, unfortunately, contains many misprints. Most of these arise in translations of titles and are unimportant, but in a considerable number of instances names of authors are misspelled or first names used instead of surnames, and in a cursory inspection several errors in dates were noted. The main text appears free from such mistakes. A serious handicap is the lack of an index. The table of contents is quite complete and detailed, but is not entirely satisfactory as an aid to finding pages for definite topics.

Edith H. Quimby

The Fundamentals of Electrocardiographic Interpretation. By J. Bailey Carter, M.D., F.A.C.P., Assistant (Rush) Professor, Department of Medicine, University of Illinois College of Medicine; Attending Staff, Cook County Hospital, Augustana Hospital, Chicago. Second edition. With a Foreword by Horatio Burt Williams, M.D., Dalton Professor of Physiology, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $6.00. Pp. 406, with 309 illustrations. Springfield, Illinois: Charles C Thomas, 1945.

The title of this book is grossly misleading for the author fails to present adequate or accurate material to justify such a resounding label on the backstrip. Over one-third of the book is given over to the electrocardiographic changes associated with myocardial infarction. Much of this material is repetitious and poorly organized since the writer reprints here six papers, dealing with this subject, which he has previously published in medical journals, presenting them as separate chapters with practically no alterations. Relatively little importance is given to the QRS changes which occur in myocardial infarction and unduly great stress is placed upon the T wave alterations in this condition. The author tends to overemphasize the value of the electrocardiogram in following the progress of a patient who has had an acute coronary thrombosis, giving it a place above that of clinical observation. Examples of the writer's misconceptions regarding the electrocardiographic changes in coronary arterial disease are such statements as "an absent R_4 or Q_5 occurs with coronary sclerosis without infarction and may occur even in the absence of coronary disease" and "rarely, if previously absent, does a deep Q_3 appear following infarction." It is stated repeatedly that inverted T waves must be present in lead II to permit the electrocardiographic diagnosis of posterior myocardial infarction, yet the author repeatedly fails to adhere to this criterion in the diagnoses accompanying his own figures.

In this work a technique for recording the

precordial electrocardiogram is recommended which consists of placing the exploring electrode in the fifth interspace in the left midclavicular line and using first the right arm and then the left leg as the indifferent electrode. The two records made in this fashion will be different only insofar as the potential variations of the indifferent electrode are different. Undoubtedly, the use of such a technique for recording chest leads accounts in large measure for the author's experience that "chest leads, in only a small percentage of cases, assist in determining the occurrence, the location, and/or duration of myocardial infarction," an experience completely dissimilar to that which the reviewers have had with quite different methods. When in support of his technique the author states, "—no other combination of chest leads is supported by such a wealth of experience. No other method for recording chest leads is so simple and fool-proof. No other lead, or combination of leads, has afforded more information in routine practice," he is either being facetious or demonstrating, further, his lack of understanding of the fundamental nature of the precordial electrocardiogram and the observations of others in this field.

A great many erroneous diagnoses accompany the figures presented with the text. A few illustrative examples are: (a) in Figure 45, right axis deviation is not present; (b) the extrasystoles in Figures 84 and 259 are of ventricular rather than of nodal origin; (c) the six sets of records in Figure 114, all of which are said to be examples of coronary occlusion, show no significant QRS changes; (d) Figures 131 and 193 are examples of left bundle branch block but show no signs diagnostic of myocardial infarction; (e) transient left bundle branch block occurs in Figure 197A but is unrecognized; (f) rather nice examples of right bundle branch block plus anterior infarction are seen in Figures 203A and B, which are said to show "early anterior (apical) infarction"; and (g) Figure 262, which is said to show complete atrioventricular heart block, actually discloses numerous responses to supraventricular impulses, thereby more properly accounting for the variations in the form of the QRS complexes.

The writer employs a "newspaper" or "telegraphic" style which may account for much of the loose writing and many of the sweeping statements made. He cannot really mean it when he says, "An iso-electric or inverted T wave in all leads is practically pathognomonic of myxedema—," or "Electrocardiograms of diabetics are seldom normal," or "A previous angina pectoris is frequently absent following coronary occlusion."

Many of the figures are too small or of too poor technical quality for careful study. Although the errors in the figures are usually recognized in the text, lead V of Figure 210E is upside down and Figures 231 and 232 are upside down and backwards. A number of typographical errors are found in the text and legends.

This book has little to recommend it except the bibliography which is rather extensive and well arranged.

Francis F. Rosenbaum
Frank N. Wilson

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DEPARTMENT OF TECHNIQUE

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DEVICE FOR SECURING PROPER ALIGNMENT IN LATERAL ROENTGENOGRAMS OF THE FEMORAL NECK

By WILLIAM P. GILMER, M.D.
Chesapeake and Ohio Hospital
CLIFTON FORGE, VIRGINIA

LATERAL views of the neck of the femur present no very difficult technical problems when the guiding anatomical points are accessible and proper alignment accurately obtained. When it is necessary to locate the pin which is being inserted for fixation of a fractured neck of the femur, the problem of accurate alignment may be difficult. It may be impossible to locate the guiding anatomical points on account of sterile sheets covering the patient. A failure to produce a satisfactory roentgenogram under these circumstances is disappointing. A very simple device for preventing these failures is described.

The device consists of a T-shaped ruler, the long arm 36 inches in length and the short arm 8 inches. The long arm is marked off in inches starting at the end which joins with the short arm (Fig. 1).

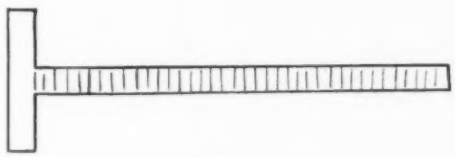

Fig. 1

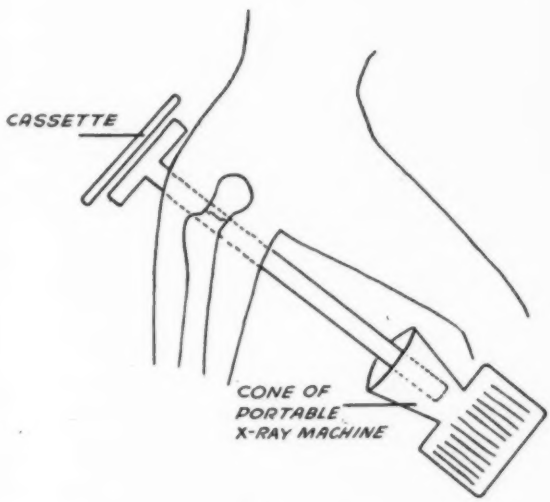

Fig. 2

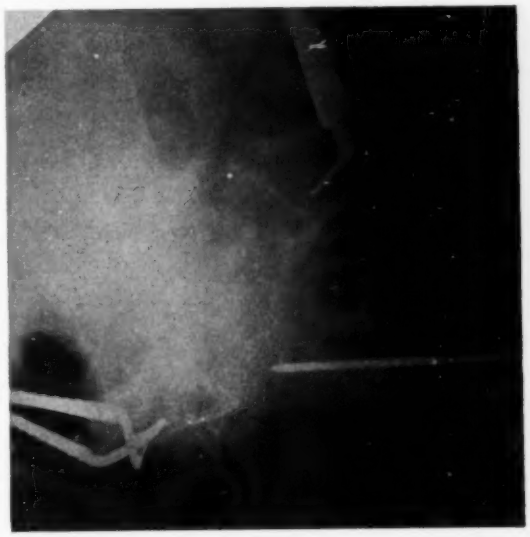

Fig. 3

The use of the ruler is quite simple. Before the operation begins and while guiding anatomical points are accessible, the ruler is placed under the patient with the long arm crossing the mid-point of the

neck of the femur at right angles to the long axis of the neck and the short arm in the position where the cassette is to be placed. With this ruler in place proper positioning of the cone of the portable roentgen machine can be quickly and accurately made. By adding the previously obtained tube cone distance to the reading on the ruler at the point to which the cone reaches the tube-film distance is obtained. By using this distance and a suitable thickness of part technique all necessity for guess work will be avoided, both as to alignment and technical factors.

Figure 2 is a sketch illustrating the use of this ruler.

Figure 3 is a roentgenogram made with a 15 ma. portable machine using the above described ruler for obtaining proper alignment.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

NECK AND CHEST

Blake, J. M. Primary carcinoma of the bronchus associated with foreign body. *Am. Rev. Tuberc.*, Jan., 1943, *47*, 109–111.

This report is concerned with a primary carcinoma of the lung which apparently developed about a small metal crucifix (measuring 4×7 mm.). This object was removed at the time of obtaining the biopsy and when the diagnosis of carcinoma was established. There was no history of aspiration of a foreign body but after detailed questioning, the patient remembered having lost the crucifix some six years previously, when he thought that he had swallowed it.

About nine months prior to the date of the biopsy, the patient had had what was thought to be an ordinary bronchitis, with severe cough, malaise, lassitude, fever up to 103°F., and some expectoration of blood-streaked sputum. Though the roentgen study was reported negative, re-examination of the roentgenogram showed a rounded density measuring about 3×3 cm. in the lower portion of the right lung.

As the fever subsided, the patient returned to his home but fatigue, cough and expectoration continued and he lost about 15 pounds. His white blood cell count reached 15,200 and there was a definite increase in the sedimentation rate. Roentgen studies indicated the presence of an atelectasis in the region where the small opacity had previously been visualized—and this led to the biopsy.—*A. A. de Lorimier.*

Hoyos, Jorge Meneses, and Quesada, J. J. Normal cardiovascular roentgen silhouette; studied by means of roentgenograms of the chests of cadavers after opaque solutions had been injected into the large vessels and chambers of the heart. *Arch. Int. Med.*, May, 1943, *71*, 666–674.

The authors have tried to determine clearly the relations that normally exist between the contour of the cardiac shadow in roentgenograms and the different chambers and large vessels of the heart. In Juarez Hospital of Mexico City, sodium iodide solution was injected into the large vessels and the chambers of the hearts of several cadavers. Roentgenograms were then taken of the chests of these cadavers placed in the dorsoventral position and in oblique position. The results of this study are given. It seems doubtful if this method of study is superior to that of angiocardiography developed by Robb and Steinberg.—*J. J. McCort.*

Crawford, J. Hamilton. Aneurysm of the heart. *Arch. Int. Med.*, April, 1943, *71*, 502–515.

Although aneurysm of the heart has been recognized for almost two centuries it is only recently that the antemortem diagnosis has been made with any assurance. The advent of

more thorough study of the patients with heart disease by roentgenologic methods has considerably increased the frequency with which the correct diagnosis is made. The author presents 13 cases, in 9 of which the diagnosis was proved at autopsy. In all of them there was well marked aneurysmal dilatation of the ventricular wall. In 4 of the group in which autopsy was performed diagnosis was made antemortem and 3 patients are still alive. One patient presented undisputable clinical evidence of the condition but permission for an autopsy could not be obtained.

Three of the patients presented here had no roentgen examination as cardiac aneurysm had not been suspected clinically. Eight showed enlargement of the heart and 3 a localized bulge. Angulation of the left ventricular wall contour was seen 3 times. Abnormal pulsations demonstrated by fluoroscopic or roentgen kymographic examination are frequently of the greatest value. Their character varies from a reversal of the normal type to absent pulsation. The pulsations were proved to be abnormal in the aneurysmal zone in 6 of these patients. Of these 4 showed an expansion during systole of the rest of the ventricle with ballooning out in a most striking manner in 2 of them; the other 2 had very small, or no pulsation. In none were pulsations of the normal type. Other authors have emphasized the value of localized pericardial adhesions in the diagnosis. This was not present in any of the cases reported here, but on autopsy adhesions to the pericardium and to the sac were seen in 6 cases. They were absent in 1, and in 2, there was no note as to its presence or absence. None of the patients in this study showed calcification in the wall of the sac or a thrombus contained therein. When calcification is seen it must be differentiated from calcification of the pericardium. The latter is on the surface and usually more diffuse, while in calcification of an aneurysm the calcification should be localized and not confined to the surface.

The roentgen examination is the most important aid in the diagnosis of cardiac aneurysm as changes in the contour can be, as a rule, clearly delineated. Unfortunately, the most common site for aneurysms is the apex which is the position in which the contour can be studied least effectively. At this point, the heart and diaphragmatic shadows mingle, which tends to obscure deformities of the cardiac contour. A diffuse, concentric apex rounded, or a broadened, blunted apex has been stated to be characteristic. These are, however, so frequently seen in patients suffering from hypertension or aortic insufficiency, which are relatively common condi ions, that it is very doubtful whether a satisfactory differentiation can be made. The apex region can be studied in more detail during very deep inspiration or after inflation of the stomach with gas.—*J. J. McCort.*

LOGUE, BRUCE R. Dissecting aneurysm of the aorta. *Am. J. M. Sc.*, July, 1943, *206*, 54–66.

Dissecting aneurysm of the aorta is a disease described as a splitting of the aorta in the media. The autopsy incidence was found to be 0.7 per cent in 1,519 autopsies from 1937 to 1940. In a study of the literature the author found that arteriosclerosis has invariably been present and it is believed that an intimal tear in an atheromatous area is the initial process.

Twelve cases that came to autopsy are presented. An antemortem diagnosis was made in 10 of the 12 cases observed and confirmed on necropsy.

The average age of the 12 patients was forty-five with a range of thirty-five to sixty-six. Ten of the 12 patients gave a history of previous cardiovascular symptoms. Eleven of the group either had hypertension on admission or gave a history of previous hypertension. The twelfth patient had a calcareous stenosis of the aortic valve.

Roentgen examination of the chest was made in 8 cases. Marked cardiac enlargement was noted in 6 instances and a moderate enlargement in 2 instances. There was a widening of the supracardiac shadow in 3 cases. A radiolucent area outside of the aorta and believed to be caused by the dissection was found in only 2 cases. A mediastinal effusion was evident in the roentgenogram of 1 patient and 1 other patient showed an extreme eccentric bulging of the heart to the right. This was due to an aneurysmal sac.

Tamponade was the cause of death in 7 cases. Hemorrhage into the pleural cavity, uremia, coronary occlusion and ventricular fibrillation were other causes of death.— *J. J. McCort.*

WEISS, SOMA, STEAD, EUGENE A., JR., WARREN, JAMES V., and BAILEY, ORVILLE T. Scleroderma heart disease; with a consideration of

certain other visceral manifestations of scleroderma. *Arch. Int. Med.*, June, 1943, *71*, 749–776.

The clinical histories of 9 patients with generalized scleroderma are reported. Postmortem examinations were performed on 2 patients. These 9 patients were selected for study because they all had symptoms and signs of heart disease. In 7 of the 9 cases the patients were women. Their ages at the onset of the cutaneous changes ranged from nineteen to sixty-two years, the average being thirty-eight years. In 3 cases the appearance of cardiac symptoms preceded changes in the skin by as much as two years. Also there were symptoms of Reynaud's disease in 8 of the 9 cases. The degree of blanching and pain in the extremities on exposure to cold could not be correlated with the progression of the visceral manifestations of the disease. Roentgen examination of the involved parts may show decalcification of bone or even loss of bony substance in the terminal phalanges and at times there may be calcified areas in the skin.

In 6 of the cases in which roentgen examination of the chest was done, strikingly similar changes were encountered. In all there was cardiac enlargement varying from a moderate to a marked degree. The heart was triangular in shape and in most cases the beat was of poor amplitude. In one instance the supracardiac area appeared to be widened and in another there was a prominent truncus pulmonaris. The roentgen findings did not suggest hypertensive or valvular heart disease. There was no detectable calcification in the valves. The left ventricle was not predominantly enlarged and the left auricle was not unduly prominent. A combination of the triangular shape and the weak heart suggested to the roentgenologist the diagnosis of myxodema heart disease or of pericardial effusion. In all of the roentgenograms there was an increase in the pulmonary markings, this usually being more marked in the lower lobe. In several cases the lungs showed a peculiar diffuse mottled or granular appearance, particularly at the bases and extending well out into the periphery but sparing the apices. At times the changes suggested to the roentgenologist the appearance of bronchiectasis or lipoid pneumonia. In instances of heart failure hilar congestion was usually noted. The focal areas of fibrosis in the lungs in 2 of the cases reported here may be related to the sclerodermatous process. It is difficult to rule out foci of chronic bronchopneumonia with organization, especially in view of the extensive lymphocytic infiltration and the peribronchial fibrosis in regions of normal alveoli. However, the distribution, corroborated by the results of roentgen examinations would be unusual in chronic bronchopneumonia.

The authors state that the lesions in the heart consist of scars of unusual type. These involve the myocardium, extending to the epicardium and endocardium only secondarily and then to a slight degree. There are certain resemblances between these lesions and those due to vascular changes. There are a number of ways, however, in which the lesions encountered postmortem in the hearts of the 2 patients with scleroderma differ from those caused by vascular disease. The lesions in the myocardium in patients with scleroderma were not in any particular relation to arteries, the structures being indifferently included in the scars or not. Furthermore the vessels were normal or showed minor intimal thickening without thrombosis or significant diminution in the caliber of the lumen. The hemosiderin deposits often seen in areas of myocardial scarring due to vascular lesions were entirely absent. Within the scars in the hearts of the 2 patients studied postmortem, the myocardial fibers were preserved in small numbers even in the center of the lesion. This was true also of fat cells and of blood vessels. The sequences were interpreted as a primary overgrowth of fibrous tissue with secondary destruction of other myocardial structures. The histopathologic nature of the lesion is different from the lesions of Fiedler's myocarditis, although their distribution is similar. The writers feel that the evidence points toward the interpretation that the myocardial lesions are an integral part of scleroderma. The pathologic observations, together with the clinical data in the cases of the series, indicated that sclerodermal heart disease is a clinical and pathologic entity.—*J. J. McCort.*

Smith, J. James, and Furth, Jacob. Fibrosis of the endocardium and the myocardium with mural thrombosis; notes on its relation to isolated (Fiedler's) myocarditis and to beriberi heart. *Arch. Int. Med.*, May, 1943, *71*, 602–619.

The authors encountered 3 cases in which

the patient died in the hospital of congestive failure of obscure origin. In all the cases the patients were carefully studied during life and examined postmortem. Clinically and pathologically these cases resemble each other closely, and without recourse to the clinical history the anatomical diagnosis might well have been isolated myocarditis. Review of the history, clinical course and histologic status, however, suggest the possibility that the changes might have been due to long continued dietary deficiency or defect in the absorption and utilization of certain acessory food factors.

Several teleroentgenograms including the anteroposterior and lateral views were made at a 2 meter distance in each case. In Case I the heart was tremendously enlarged and all diameters, particularly that of the left ventricle and the pulmonary artery, appeared full. A small amount of fluid obscured the left costophrenic angle. The heart in Case II was increased to the right and the left with a straightening of the left cardiac border, the left ventricle constituting the major enlargement. On roentgen examination of Case III the transverse diameter of the heart was increased, the enlargement being mainly left ventricular and the pulmonary artery was so prominent that mitral stenosis was suggested. Considerable fluid was apparent in the right pleural space with extension into the minor fissure.

The principal findings at necropsy in these cases agreed in several respects. In each there was evidence of cardiac failure with chronic passive congestion of the viscera. Pulmonary infarction was encountered in 2 cases while in the third there were small renal infarcts. The heart was enlarged in each case, weighing 650, 500 and 460 gm. respectively. Mural thrombi with varying degrees of organization were seen in both right and left ventricles in 2 cases, while the left ventricle alone was involved in the third. There was no anatomic evidence of valvular defects, hypertension, arteriosclerosis or syphilis. Myocardial fibrosis was the conspicuous microscopic change. The most marked feature in all cases was the widespread endocardial fibrosis in both right and left ventricles, varying in its extremes from plaque-like deposits to the formation of a dense fibrous tissue plaque covering the myocardium and investing the papillary muscles and trabeculae carneae.

The patients, 2 men and 1 woman, were thirty-five to forty years of age. In 1 case symptoms were present during eight years with the final phase of the illness occupying twelve months. In the other 2 cases the patients were ill for eight and nine months, respectively. In each there was progressive decline modified slightly by therapeutic measures. One patient, a Chinese man, had lived on a deficient diet over a long period; the other 2 patients had poor appetites and had taken diets probably border line in their content of the vitamin B complex. In all cases the diet was deficient after the onset of the final illness. Whether the cases here described actually represent chronic beriberi heart or at all the consequence of nutritional deficiency is not adequately proved. However, the question is raised whether these changes could have been associated with deficient diet and could represent a variant of beriberi heart.—*J. J. McCort.*

Dr. W. C. Röntgen